RISK ESTIMATES FOR NONSMOKER LUNG CANCER BASED UPON MODELING PROCEDURES

- In 1985, Repace and Lowrey published an article claiming that exposure to ETS is responsible for 500 to 5,000 lung cancer deaths per year in the United States.[1] This report received extensive press coverage upon its release.

- The report contains two highly theoretical models for estimating risks of lung cancer from ETS exposure. One model relies upon a "reinterpretation" of the epidemiologic studies of lung cancer in nonsmokers; the second model estimates lung cancer mortality among nonsmokers based on a single study dealing with the Seventh Day Adventists, a religious group known for its vigorous opposition to smoking.

- Critics of the Repace and Lowrey approach have pointed out that the estimates are based on errors and "unrealistic assumptions" which result in overestimations of exposure.[2] One analysis of the model showed that, depending on the assumptions and input data used, the estimates are inherently inaccurate and may vary by as much as 300-fold.[3] Another scientist noted that the exposure and dose levels used in the modeling exercise were not based on actual measurements; such measurements reported elsewhere range from "ten- to one-hundred-fold less than that in the Repace and Lowrey model."[4]

2500061531

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

- Other criticisms have focused on the report's methods of analysis,[5-7] and suggest that Repace and Lowrey failed to control for other confounding factors, and that their model did not provide "the very statistical bases of estimation procedures."[4]

- Repace and Lowrey's estimate of nonsmoker lung cancer risks in the workplace was also criticized by scientists who noted that none of the epidemiologic studies of ETS exposure and disease in nonsmoking working women report a statistically significant increase in risk.[2]

- Two British researchers, Darby and Pike, published a paper in 1988 describing another type of mathematical model which predicted potential effects from ETS exposure based on data from a study on active smoking.[8] Even when adjustments were made for childhood exposure to ETS, the authors reported that the model predicted a risk for nonsmokers that was smaller than "the underlying background risk for lung cancer." They concluded that their model could not explain the difference between risks reported for nonsmokers in epidemiologic studies and the low levels of ETS exposure reported in other studies.

2500061532

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

- The Darby and Pike model was criticized in 1990 by Wald, et al., authors of one of the earlier meta-analyses on the epidemiologic studies of ETS exposure and lung cancer incidence.[9] Wald's group questioned Darby and Pike's conclusion that there was a discrepancy between risks estimated by epidemiologic studies and by exposure data. Darby and Pike replied that the existing cotinine data employed by Wald, et al., were possibly both insufficient and inappropriate to allow an adequate comparison to be made with the epidemiologic data.[10]

2500061533

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

REFERENCES

1. Repace, J.L. and Lowrey, A.H., "A Quantitative Estimate of Nonsmokers' Lung Cancer Risk from Passive Smoking," Environment International 11(1): 3-22, 1985.

2. Arundel, A., Irwin, T. and Sterling, T., "Nonsmoker Lung Cancer Risks from Tobacco Smoke Exposure: An Evaluation of Repace and Lowrey's Phenomenological Model," Journal of Environmental Science and Health C4(1): 93-118, 1986.

3. Arundel, A., Sterling, T. and Weinkam, J., "Never Smoker Lung Cancer Risks from Exposure to Particulate Tobacco Smoke," Environment International 13: 409-426, 1987.

4. Lebowitz, M.D., "The Potential Association of Lung Cancer with Passive Smoking," Environment International 12: 3-9, 1986.

5. Johnson, C. and Letzel, H., "Letter to the Editors," Environment International 12: 21-22, 1986.

6. Burch, P.R.J., "Health Risks of Passive Smoking: Problems of Interpretation," Environment International 12: 23-28, 1986.

7. Kilpatrick, S.J., "Letter to the Editors," Environment International 12: 29-31, 1986.

8. Darby, S.C. and Pike, M.C., "Lung Cancer and Passive Smoking: Predicted Effects from a Mathematical Model for Cigarette Smoking and Lung Cancer," British Journal of Cancer 58: 825-831, 1988.

9. Wald, N., Nanchahal, K., Cuckle, H. and Thompson, S., "Letter to the Editor: Lung Cancer and Passive Smoking," British Journal of Cancer 61: 337, 1990.

10. Darby, S.C. and Pike, M.C., "Response to the Letter from Dr. Wald," British Journal of Cancer 61: 337-338, 1990.

2500061534

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

ETS AND CANCER OF SITES OTHER THAN THE LUNG

Introduction

A presenter at the recent McGill Symposium in Montreal, Canada, described the then-available epidemiologic studies on ETS and cancer other than the lung as follows:

> These nine studies provide insufficient data to evaluate the effect of ETS on cancer other than of the lung. The reported associations are weak and inconsistent, and are subject to the potential effects of biases and uncontrolled confounding factors . . .[1]

These studies concern a variety of cancer sites; the publications on each are briefly summarized below. Highlighted copies of the papers on cancer at other sites are found at Tabs 1-11.

All Cancers Combined

- Several studies have presented risk estimates for overall cancer incidence, regardless of site, among individuals reporting ETS exposure. This procedure disregards differences in etiology, mechanism and confounding factors among the various types of cancer; nevertheless, some authors have presented data in this fashion.

Hirayama (1984) reported a significant elevation in risk for "cancer of all sites," in nonsmoking women whose husbands

2500061535

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

smoked; he attributed the elevation to increased risks for lung, nasal sinus, and brain cancers.[2]

Miller (1984) reports on a "case-control" study conducted in Pennsylvania by interviewing the surviving relatives of women whose death notices were published in a local newspaper.[3] Miller reported an overall odds ratio of 1.40 for "death due to cancer" among women whose husbands smoked. Questions can be asked about the accuracy of the amount of recall required of the relatives in this study.

In an abstract, Reynolds, et al., (1987) reported that a record-linkage study in Alameda County, CA concluded that nonsmoking women married to smokers had a 70% higher risk of cancer incidence at all sites, and that they had an approximate relative risk of 7.0 for "smoking-related cancers."[4] The abstract provides insufficient information to judge the quality of the study; the reported risk estimates should be viewed with caution.

Sandler, et al., (1989) reported statistically nonsignificant point estimates of 1.01 (males) and 1.00 (females) for all cancers in persons reporting ETS exposure.[5] The authors' subdivision of the category into "smoking-related" and "other" cancers yielded no statistically significant risk estimates. This study was criticized by Holcomb (1989) as being "poor science" and

2500061536

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

"inadequately designed."[6]

Brain and Nasal Sinus Cancers

- A single report claims to show an increased risk for brain and nasal sinus cancers associated with marriage to a smoker. No other researchers have been able to replicate these findings and they must be considered isolated.

Only Hirayama (1984), reporting further on his study of Japanese women, has reported statistically significant associations in women between brain and nasal sinus cancers and spousal smoking.[2]

Breast Cancer

- Some claims have been made for a relationship between husband's smoking and breast cancer in nonsmoking women.

Sandler, et al., (1985) reported a statistically non-significant increased risk for breast cancer in non-smoking women and statistically significant elevated risks for cancers of the endocrine system associated with early life (i.e., childhood) exposure to parental smoking.[7]

2500061537

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Hirayama (1984), in his discussion of his claim that his data support an elevated risk for all cancers in nonsmoking women whose husbands smoke, suggested that part of the reported increase might be due to breast cancer.[2] In a 1991 article, Wells reports a statistically nonsignificant increased risk of breast cancer using additional data supplied by Hirayama.[8]

Bladder Cancer

- Two case-control studies have specifically examined bladder cancer incidence; neither reported an association between bladder cancer and exposure to ETS at home or at work.

The 1986 Kabat, et al., paper reported that cases and controls in this study did not differ significantly in reporting "sidestream smoke exposure" at home, at work or in transportation.[9] Neither did they differ significantly in whether or not their spouse smoked. The authors concluded that "exposure to sidestream smoke" is not an important factor in bladder cancer in nonsmokers.

The second study to report on bladder cancer is by Burch et al. (1989).[10] It was conducted in Alberta and Ontario, Canada. None of the reported relative risks was statistically significant. The authors concluded that there was no evidence for an effect of

2500061538

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

"passive smoking" on bladder cancer incidence in smokers or nonsmokers.

Cervical Cancer

- Two studies have reported on ETS exposure and the incidence of cervical cancer. Both fail to account sufficiently for confounding factors.

Statistically significant elevated risks for cervical cancer were reported in a 1985 study by Sandler, et al., of patients in North Carolina.[11] This study has been criticized because it did not control for known risk factors such as sexual activity, which is strongly correlated with incidence of cervical cancer.

Slattery, et al., (1989), in a study of women in Utah, reported a statistically significant increased risk of cervical cancer in non-smokers who reported three or more hours of ETS exposure per day (risk estimate of 3.43, 95% CI 1.23-9.54).[12] Although the researchers adjusted for age, church attendance, education and number of sexual partners, these variables do not account for all factors that may contribute to disease.

2500061539

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Zang, Wynder and Harris authored a letter in response to the Slattery, et al., study.[13] They wrote:

> [T]here clearly is undermatching of control patients with regard to important risk factors including sexual activity, religious background, and education. . . . Since the previously mentioned risk factors are correlated highly with one another as well as with active and passive smoking, the risk estimates relating smoking and cervical cancer may be subject to substantial bias and confounding. . . . In fact, the adjusted odds ratios are probably no more than the leftover effect of variables controlled imperfectly by logistic regression.

In a response, Slattery acknowledged that her group's conclusions "should be verified in other studies."[14]

Childhood Cancers

- Two papers have claimed that their data show that childhood exposure to ETS is related to increased incidence of certain childhood cancers.

Grufferman, et al., (1982) reported a statistically significant relative risk of 3.9 (95% CI 1.5-9.6) for father's cigarette smoking for childhood rhabdomyosarcoma in a case-control study in North Carolina.[15] Only 33 cases were included in the study; only 23 cases were included in the analysis of father's smoking. Conversely, for the 8 cases with maternal smoking, the reported relative risk was 0.8 (95% CI 0.3-2.0). An extremely

2500061540

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

large number of analyses was conducted in this study, suggesting the possibility of data-dredging.

A recent study (John, et al., 1991) reported associations for father's smoking during pregnancy (i.e., a surrogate for ETS exposure of the pregnant woman) in the absence of maternal smoking, with several indices of childhood cancer: all cancers combined (OR = 1.2, 95% CI 0.8-2.1), acute lymphocytic leukemia (OR = 1.4, 95% CI 0.6-3.1), lymphomas (OR = 1.6, 95% CI 0.5-5.4) and brain cancer (OR = 1.6, 95% CI 0.7-3.5).[16] Not one of the associations was statistically significant.

Conclusion

- The studies concerning ETS exposure and cancer other than of the lung are few in number and subject to the same criticisms applicable to the lung cancer studies, e.g., "data-dredging," no assessment of exposure, inadequate control for confounding factors. Additionally, there are only one or two reports on a given cancer endpoint. Without replication of the results, it is not possible to reach any conclusion about ETS exposure and non-pulmonary cancer incidence.

2500061541

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

REFERENCES

1. Layard, M.W., "Environmental Tobacco Smoke and Cancer: The Epidemiologic Evidence," Environmental Tobacco Smoke: Proceedings of the International Symposium at McGill University 1989, eds. D. Ecobichon and J. Wu, (Lexington, Massachusetts: Lexington Books, 1990): 99-115.

2. Hirayama, T., "Cancer Mortality in Nonsmoking Women with Smoking Husbands Based on a Large-Scale Cohort Study in Japan," Preventive Medicine 13: 680-690, 1984.

3. Miller, G.H., "Cancer, Passive Smoking and Nonemployed and Employed Wives," The Western Journal of Medicine 140: 632-635, 1984.

4. Reynolds, P., Kaplan, G.A. and Cohen, R.D., "Passive Smoking and Cancer Incidence: Prospective Evidence from the Alameda County Study," (abstract) American Journal of Epidemiology 126(4): 767, 1987.

5. Sandler, D.P., Comstock, G.W., Helsing, K.J. and Shore, D.L., "Deaths from All Causes in Non-Smokers Who Lived with Smokers," American Journal of Public Health 79: 163-167, 1989.

6. Holcomb, L.C., "Risk to Passive Smokers," (letter to the editor) American Journal of Public Health 79(10): 1432, 1989.

7. Sandler, D.P., Everson, R.B., Wilcox, A.J. and Browder, J.P., "Cancer Risk in Adulthood from Early Life Exposure to Parents' Smoking," American Journal of Public Health 75(5): 487-492, 1985.

8. Wells, A.J., "Breast Cancer, Cigarette Smoking, and Passive Smoking," (letter to the editor) American Journal of Epidemiology 133(2): 208-210, 1991.

9. Kabat, G.C., Dieck, G.S. and Wynder, E.L., "Bladder Cancer in Nonsmokers," Cancer 57: 362-367, 1986.

10. Burch, J.D., Rohan, T.E., Howe, G.R., Risch, H.A., Hill, G.B., Steele, R. and Miller, A.B., "Risk of Bladder Cancer by Source and Type of Tobacco Exposure: A Case-Control Study," International Journal of Cancer 44: 622-628, 1989.

11. Sandler, D.P., Everson, R.B. and Wilcox, A.J., "Passive Smoking in Adulthood and Cancer Risk," American Journal of Epidemiology 121: 37-48, 1985.

2500061542

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

12. Slattery, M.L., Robison, L.M., Schuman, K.L., French, T.K., Abbott, T.M., Overall, J.C. and Gardner, J.W., "Cigarette Smoking and Exposure to Passive Smoke Are Risk Factors for Cervical Cancer," Journal of the American Medical Association 261: 1593-1598, 1989.

13. Zang, E.A., Wynder, E.L. and Harris, R.E., "Exposure to Cigarette Smoke and Cervical Cancer," (letter to the editor) Journal of the American Medical Association 262(4): 499, 1989.

14. Slattery, M.L., "Exposure to Cigarette Smoke and Cervical Cancer: In Reply," (letter to the editor) Journal of the American Medical Association 262(4): 499, 1989.

15. Grufferman, S., Wang, H.H., DeLong, E.R., Kimm, S.Y.S., Delzell, E.S. and Falletta, J.M., "Environmental Factors in the Etiology of Rhabdomyosarcoma in Childhood," Journal of the National Cancer Institute 68(1): 107-113, 1982.

16. John, E.M., Savitz, D.A. and Sandler, D.P., "Prenatal Exposure to Parents' Smoking and Childhood Cancer," American Journal of Epidemiology 133(2): 123-132, 1991.

2500061543

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

ETS and Heart Disease

Introduction

This notebook discusses and provides copies of the public literature bearing directly on the claim that environmental tobacco smoke (ETS) is related to heart disease. Most of this literature is epidemiological, with a current total of 11 studies presenting data on a possible statistical association between ETS and heart disease incidence or mortality.

These epidemiological reports are important because they are the primary basis for claims of an elevated heart disease risk in nonsmokers exposed to ETS. However, the literature also contains claims of special harm in compromised individuals, such as heart disease patients, or regarding biochemical effects that might mediate an adverse effect of ETS on heart disease incidence or mortality. Accordingly, this notebook also includes several laboratory and statistical reports dealing with ETS and exercise performance, particularly in angina patients, or with biochemical factors suggested as involved in the development of heart disease.

Each of the articles included in this notebook has been highlighted in blue and yellow. The blue highlighting identifies the most notable comments supporting a relationship of ETS with heart disease, or that are otherwise adverse regarding tobacco or smoking. The yellow highlighting identifies comments that

2500061544

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

challenge, or at least that are concessionary concerning, the potential involvement of ETS or tobacco in disease causation.

The initial section of this notebook contains an overview and discussion of the literature. The literature itself is grouped into four appendices. Appendix A (Tabs 1-13) contains the primary epidemiological reports, consisting of 11 studies reported in 13 articles. A summary and discussion of major criticisms is provided for each individual study. Appendix B (Tabs 14-17) contains the major meta-analyses and reviews concluding that ETS is associated with an elevated heart disease risk. Appendix C (Tabs 18-23) contains the primary reviews which have judged that the data are inadequate to conclude that ETS is related to heart disease. Appendix D (Tabs 24-35) contains a mixed group of articles which provide data concerning ETS in relation to exercise performance, potential effects in heart patients or in relation to cardiovascular biochemical and cellular processes. Short summaries are provided with the articles in Appendix D. If notable letters to the editor or other editorial comments were published concerning any of the articles in this notebook, these materials were also included.

2500061545

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Epidemiologic Reports and Reviews

Reports with original data

There are currently 11 studies (in 13 reports) presenting epidemiological data on a possible statistical association between ETS and heart disease incidence and mortality. There are 13 reports, because for two studies, the data were presented in two separate articles. It should be emphasized, however, that the epidemiological reports on the heart disease issue include several scientifically weak sources, particularly meeting abstracts. Furthermore, all of these studies are open to serious methodological criticisms. Summaries of the individual studies, as well as a list of the major criticisms of each, are provided with the highlighted copies of the articles in Appendix A.

The ETS associated risks reported in the 11 epidemiological studies are summarized in the following table.

2500061546

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

ETS/Heart Disease Epidemiological Reports

	Sex	Reported Risk	Statistical Testing
Butler (1990)[1]	F	RR = 1.40	0.51 - 3.84 (95% CI)
Garland et al. (1985)[2]	F	RR = 2.7	$p \leq .10$
		Ctrl vs. ETS	
Gillis et al. (1984)[3]	M	31 vs 45 per 10^4/yr	No stat. test rpted.
	F	4 vs 12 per 10^4/yr	No stat. test rpted.
*He, et al. (1989)[4]	F	OR = 1.50	$p < .01$
*Helsing, et al. (1988)[5]	M	RR = 1.31	1.1-1.6 (95% CI)
	F	RR = 1.24	1.1-1.4 (95% CI)
Hirayama (1984)[6]	F (husbands smoking $\geq$ 20 cigs/day)	RR = 1.31	1.06-1.63 (90% CI)
*Hole, et al. (1989)[7]	M+F	RR = 2.01	1.21-3.35 (95% CI)
Humble, et al. (1990)[8]	F	RR = 1.59	0.99-2.57 (95% CI)
Lee, et al. (1986)[9]	M+F	RR = 1.03	0.65-1.62 (95% CI)
*Martin, et al. (1986)[10]	F	RR = 3.4	$p < .01$
Palmer, et al. (1988)[11]	F	RR = 1.2	No stat. test rpted.
*Sandler, et al. (1989)[12]	M	RR = 1.31	1.05-1.64 (95% CI)
	F	RR = 1.19	1.04-1.36 (95% CI)
Svendsen, et al. (1987)[13]	M	RR = 2.23	0.72-6.92 (95% CI)

NOTE: Gillis, et al. (1984) and Hole, et al. (1989) are based on the same study. Also, Helsing, et al. (1988) and Sandler, et al. (1989) are based on the same study.

*Reported to be statistically significant at the 95% level of confidence.

2500061547

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

In an overall evaluation of the epidemiological reports, it is important to consider the issue of statistical significance. Some fluctuation in disease or mortality rates will occur simply by chance alone. Hence, when these rates are compared, as in risk ratios, it is necessary to apply a standard to determine the statistical likelihood that an apparent elevation or reduction in risk reflects chance variation or whether it reflects an actual difference in the comparison groups. The traditional scientific standard is to require that a statistical test indicate at least a 95% probability that an observed difference reflects a true effect. Stated in reverse, this would mean that the standard only allows a 5% probability that the result was due to chance.

When discussing relative risks, if the disease or mortality rates are equivalent in the comparison groups, this will be reflected in a ratio of 1.0. When a statistical test is performed, the 95% standard is met when the 95% confidence intervals are reported not to include 1.0. Sometimes a "p" value is given, which states the probability that an observation is due to chance. Hence, a statement of "p < .05" means that the observation could have occurred by chance less than 5% of the time. To state "p < .05" or to provide 95% confidence intervals that do not include 1.0, are equivalent indications of statistical significance.

2500061548

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Only four of the 11 epidemiological studies regarding ETS and heart disease report a statistically significant result at the 95% level of confidence. (1) He, et al. (1989), a Chinese language report based on only 34 female heart disease patients; (2) Helsing, et al. (1988)/Sandler, et al. (1989), a study based on a Maryland census in which the information regarding spousal smoking (used to estimate ETS exposure) was from 1963; (3) Hole, et al. (1989), a Scottish study based on only 84 heart disease deaths; and (4) Martin, et al. (1988), a report based on 23 women who reported having a heart attack and which was given a conference but apparently not otherwise accepted for publication.

In sum, seven of the 11 studies of ETS exposure and heart disease have failed to report a statistically significant association. In the four studies that have claimed a statistically significant relationship, two were from outside the United States. Three were very small-scale. All of these studies suffer from a variety of serious methodological weaknesses.

A list of the most common weaknesses in the individual studies is provided below. It will be recognized that these are characteristic of epidemiological studies of ETS in general, not simply those relating to heart disease. For a more detailed discussion of the criticisms applicable to each study, see Appendix A.

2500061549

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

1. Small sample sizes.

2. Lack of statistical significance, or failure to test for statistical significance.

3. Potential misclassification of the smoking status of study participants.

4. Inadequate assessment of ETS exposure.

5. Failure to control adequately for biases stemming from potential confounding variables.

6. Failure to confirm causes of death via autopsy or other histological methods.

Reviews claiming ETS-associated risk

Despite the scientific weaknesses in the epidemiologic literature on ETS and heart disease, four recent reviews have concluded that ETS is associated with an increased risk of heart disease and that, in fact, such exposure causes a large number of deaths each year. Copies of these reviews are provided in Appendix B. Each of these reviews attempted to estimate an overall risk based on the combined data from the epidemiologic studies. These estimated risk ratios and the associated 95% confidence intervals are provided in the following table.

2500061550

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Meta-Analyses and Reviews of ETS-Heart Disease Data

		RR	95% CI
Wells (1988)[14]	Males	1.31	(1.1-1.6)
	Females	1.23	(1.11-1.36)
	Home		
Kawachi, et al. (1989)[15]	Males	1.3	(1.1-1.6)
	Females	1.2	(1.1-1.4)
	Workplace		
	Males	2.3	(1.4-3.4)
	Females	1.9	(1.4-2.5)
Kristensen (1989)[16]	Both sexes	≈ 1.3	
Glantz and Parmley (1991)[17]	Both sexes	1.3	(1.2-1.4)

These estimates were generally derived from the statistical technique known as meta-analysis. (The Kristensen article appears to be an exception, in that the estimated 1.3 relative risk was apparently based on an informal estimation and no confidence intervals were given.) Although these reviews varied somewhat in form, detail and focus, the estimates were generally similar, about 1.3, reflecting a 30% elevation in risk associated with ETS exposure.

The Kawachi, et al. (1989) discussion was fairly narrowly focused on New Zealand. The Kristensen (1989) discussion was a

2500061551

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

limited part of a larger discussion of factors involved in cardiovascular diseases and the work environment. Thus, the major reviews, both of which clearly involved meta-analytic techniques, were those by Wells in 1988 and by Glantz and Parmley in 1991. These two reports are discussed further below.

A. Judson Wells, a consultant to the American Lung Association, statistically combined the data from several reports on ETS and heart disease, including both prospective (cohort) and case-control studies. He then calculated overall relative risks (ETS exposed versus nonexposed) for lung cancer (1.44 for females; 2.1 for males), cancers other than lung (1.16 for females; no risk elevation for males) and heart disease (1.23 for females; 1.31 for males). He also estimated numbers of death related to these disease categories, claiming that ETS exposure results in 46,000 deaths per year in nonsmokers. Of these, 3,000 are claimed to be from lung cancer. For cancers other than the lung, he calculated that ETS exposure results in 11,000 annual deaths. The largest number of deaths from ETS exposure was claimed to be due to heart disease. He claimed that 32,000 nonsmoker heart disease deaths per year stem from ETS exposure.

The most recent, and certainly the most widely publicized, review of ETS and heart disease was undertaken by two authors from the Department of Medicine, University of California, San Francisco.

2500061552

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

In their 1991 paper, Stanton Glantz and William Parmley conclude that ETS exposure is statistically associated with an estimated 30% increase (relative risk of 1.3) in heart disease risk in nonsmokers. They argue that this translates into 37,000 heart disease deaths in nonsmokers stemming from ETS exposure. Glantz and Parmley also discuss a number of biochemical and experimental studies which purportedly support the biological plausibility of such a relationship.

In evaluating the claims by Wells and by Glantz and Parmley, it should be emphasized that meta-analysis, the technique from which they derive their risk estimates, is appropriately used only when the underlying studies are highly similar and of high quality. If the underlying studies are based on different populations and procedures and suffer from serious methodological weaknesses, then any meta-analysis will consequently be invalidated.

The above considerations are directly applicable to an evaluation of the risk claims regarding ETS and heart disease. These claims are based on meta-analyses of a small group of epidemiological studies reporting a relationship between ETS exposure and an increased risk of heart disease. In general, these studies deal with spousal smoking and assess heart disease risk in the nonsmoking spouse. Otherwise, these studies used widely disparate methodologies, study populations and endpoints. Several

2500061553

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

are very weak, preliminary, available only in abstract form, or are based on such scanty data that they quite arguably are not sufficiently reliable or valid even to be considered seriously in a meta-analysis. Appendix A contains discussions of the major flaws in the individual studies.

Reviews emphazing inconclusiveness of the data

Reviews such as those by Wells and by Glantz and Parmley often receive a great deal of publicity. However, it is important to recognize that there have been a number of other examinations of the data concerning ETS and heart disease. Several important reviews have concluded that the data on this issue are equivocal and inadequate to support claims of an increased heart disease risk in nonsmokers exposed to ETS.

The first major reviews of the epidemiological data on ETS and heart disease appeared in 1986. In that year, a report of the United States Surgeon General[18] examined the available data and judged that "no firm conclusion" (p. 10) could be made regarding a possible relationship between ETS and heart disease. Also in 1986, a similar evaluation appeared from a committee of the National Research Council of the National Academy of Sciences.[19] This committee calculated that any potential heart disease risk related to ETS would be "difficult to detect or estimate reliably" from

2500061554

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

epidemiological studies, and would be "the same order of magnitude as what might arise from expected residual confounding due to unmeasured covariates." (p. 263)

Thus, both the 1986 Surgeon General's Report and the National Research Council report judged that the data were insufficient to allow a conclusion that ETS exposure is a cause of heart disease. Even the 1991 review by Glantz and Parmley recognized this as a "reasonable" position, at least in 1986. On the other hand, Glantz and Parmley argued that data published since 1986 warrant that this conclusion be modified. However, other scientists have undertaken more balanced and critical reviews of the more recent data and have judged that it remains inconclusive. The four most significant of these reviews, and their conclusions, are as follows:

a. At a major conference on ETS held at McGill University in 1989, Lawrence Wexler, of the New York Medical College, concluded that recent data did not provide a basis for altering the earlier conclusions by the Surgeon General and National Research Council concerning ETS and cardiovascular disease.

> Based on the available evidence, it is this author's opinion that it has not been demonstrated that exposure to ETS increases the risk of cardiovascular disease. (p. 139)[20]

2500061555

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

b. A similar evaluation was made by two scientists from the United Kingdom, who reviewed the literature on ETS and heart disease and presented their conclusions at an international conference on indoor air quality held in Lisbon, Portugal in April 1990.

> It is concluded that no increased risk of cardiovascular disease can be associated unequivocally with exposure to ETS, and it seems probable that this will continue to be the case until specifically designed trials are instigated, and some objective measure of degree of exposure can be devised. (p. 215)[21]

c. Another scientific review of this literature was performed by two physicians from the University of Munich, Germany and given at an international conference in Hungary in June 1990. The conclusion was similar.

> Taking into account the small increase in coronary risk in passive smokers as compared to non-exposed subjects and also the low validity and small number of epidemiological studies available and the fact that their results are at least inconsistent, a relationship between passive smoking and cardiovascular diseases cannot be established on these data. (p. 6)[22]

d. In a 1991 book discussing a wide range of issues involving ETS, the literature on heart disease was reviewed by Alan Armitage, former director of toxicology of a major European research laboratory and now head of pharmacology at

2500061556

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

the Tobacco Research Council Laboratories in the United Kingdom. He judged that the scientific data have not established an increased heart disease risk in nonsmokers exposed to ETS.

> It is clear that the evidence for a harmful effect of ETS in enhancing CHD [coronary heart disease] risk in non-smokers is not very convincing. . . . (p. 114)[23]

Studies Involving Exercise Performance, Heart Disease Patients and Biochemical Measurements

There are several experimental and biochemical studies that have been cited in the literature as supporting an increase in heart disease risk stemming from ETS exposure. A few of these reports claim that ETS exposure adversely effects exercise capacity and that in the case of heart disease patients, this can lead to attacks of angina (heart pain). Other reports have attempted to demonstrate that ETS exposure adversely affects some aspect of cardiovascular function, such as blood clotting (platelets), myocardial respiration (oxygen usage) or cholestol levels. These articles, with brief summaries, are provided in Appendix D.

In an overall evaluation of these studies, it is important to note that they constitute a relatively minor aspect of the ETS/heart disease issue. That is, the claim that ETS increases the risk of heart disease is a statistical statement based on epidemiological reports. Once having made that statement, various

2500061557

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

kinds of studies dealing with cardiovascular or exercise performance or with mechanisms might be marshalled to argue for its plausibility. On the other hand, without the epidemiological underpinning, such studies would probably be much less notable since there would be nothing that they would be attempting to explain.

In the area of exercise performance, there are three primary studies. In one of these, a 1985 report by McMurray, et al.,[24] healthy subjects were used and ETS exposure was claimed to have an adverse effect on exercise performance. Two other studies, one by Aronow (1978)[25] and the other by Khalfen and Klochkov (1987)[26] used angina patients. In somewhat similar study designs, both reports claimed that when these heart disease patients were exposed to ETS, they were not able to exercise as long before experiencing angina. The credibility of the Aronow report has been widely challenged in the literature. The Khalfen and Klochkov report is a Russian language article about which relatively little is known. Regarding any of the exercise performance studies, whether with healthy or heart disease patients, a general criticism is that when dealing with ETS, it is almost impossible to "blind" either the experimenter or the subjects with regard to ETS exposure. Thus, the possibility is always open that some subjective factor may influence the results.

2500061558

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

There are very limited data attempting to demonstrate that ETS adversely affects some process that might be involved in blood clotting (thrombus formation) or atherosclerosis. The primary focus has been on the possibility that ETS may increase the tendency of certain blood components, known as platelets, to stick together. This claim has been made based mainly on data in four published reports. Three of these are from the same Austrian research group. (Sinzinger and Kefalides, 1982[27]; Burghuber, et al., 1986[28]; Sinzinger and Virgolini, 1989[29]) Of these three, one is merely a letter to the editor (Sinzinger and Kefalides, 1982) and another is a German language article with only an English abstract (Sinzinger and Virgolini, 1989). The fourth report, Davis, et al., (1989)[30] is from a group of researchers in Kansas City, Missouri. It suffers from serious methodological weaknesses, particularly its failure to establish a proper control condition.

Finally, there are two reports of children which assessed cholesterol and other blood components in relation to parental smoking status (Moskowitz, et al., 1990[31]; Pomrehn, et al., 1990[32]), one of which (Pomrehn, et al., 1990) is only available as an abstract from a meeting presentation. Both reports claimed that parental smoking was associated with decreases in HDL cholesterol, which some literature has argued may be associated with heart disease risk. These studies measured components of blood as the endpoint, but are essentially epidemiological studies in that they,

2500061559

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

at best, may suggest statistical correlations. As such, they suffer from weaknesses characteristic of other epidemiological studies of ETS exposure, especially difficulties in controlling for potential confounding variables and inadequate assessment of ETS exposure. Furthermore, the potential significance of blood values in relation to later heart disease risk in a group of children is highly speculative.

This notebook also contains a group of three articles relating to research from a Czechoslovakian group, which claims that "passive smoking" has an adverse effect on the heart's use of oxygen.[33] [34] [35] These were animal studies involving smoke exposure to rabbits. They clearly involved a design intended to mimic "active" smoking, and are included in this notebook merely because they were erroneously discussed in the 1991 Glantz and Parmley paper as providing data relevant to ETS exposure.

WLS/tks

2500061560

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Endnotes

1. Butler, T., "The Relationship of Passive Smoking to Various Health Outcomes Among Seventh-Day Adventists in California," Presented at the Seventh World Conference on Tobacco and Health, Abstract, 1990.

2. Garland, C., Barrett-Connor, E., Suarez, L., Criqui, M.H. and Wingard, D.L., "Effects of Passive Smoking on Ischemic Heart Disease Mortality of Nonsmokers: A Prospective Study," American Journal of Epidemiology 121(5): 645-650, 1985.

   Garland, C., Barrett-Connor, E., Suarez, L., Criqui, M.H. and Wingard, D.L., "Effects of Passive Smoking on Ischemic Heart Disease Mortality of Nonsmokers: A Prospective Study," Erratum, American Journal of Epidemiology 122: 1112, 1985.

3. Gillis, C.R., Hole, D.J., Hawthorne, V.M. and Boyle, P., "The Effect of Environmental Tobacco Smoke in Two Urban Communities in the West of Scotland." In: ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.C. Snella (eds.). European Journal of Respiratory Diseases, Supplement No. 133, Vol. 65, 121-126, 1984.

4. He, Y., et al., "Women's Passive Smoking and Coronary Heart Disease," Chung Hua Yu Fang I Hsuch Tsa Chih 23(1): 19-22, 1989.

5. Helsing, K.J., Sandler, D.P., Comstock, G.W. and Chee, E., "Heart Disease Mortality in Nonsmokers Living With Smokers," American Journal of Epidemiology 127(5): 915-922, 1988.

6. Hirayama, T., "Lung Cancer in Japan: Effects of Nutrition and Passive Smoking." In: Lung Cancer: Causes and Prevention. M. Mizell and P. Correa (eds.). New York, Verlag Chemie International, Chapter 14, 175-195, 1984.

7. Hole, D.J., Gillis, C.R., Chopra, C. and Hawthorne, V.M., "Passive Smoking and Cardiorespiratory Health in a General Population in the West of Scotland," British Medical Journal 299: 423-427, 1989.

8. Humble, C., Croft, J., Gerber, A., Casper, M., Hames, C.G. and Tyroler, H.A., "Passive Smoking and 20-Year Cardiovascular Disease Mortality among Nonsmoking Wives, Evans County, Georgia," American Journal of Public Health 80(5): 599-601, 1990.

10381016

2500061561

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

9. Lee, P.N., Chamberlain, J. and Alderson, M.R., "Relationship of Passive Smoking to Risk of Lung Cancer and Other Smoking-Associated Diseases," British Journal of Cancer 54: 97-105, 1986.

10. Martin, M.J., Hunt, S.C. and Williams, R.R., "Increased Incidence of Heart Attacks in Nonsmoking Women Married to Smokers," Presented at the Annual Meeting of the American Public Health Association, Abstract, 1986.

11. Palmer, J.R., Rosenberg, L. and Shapiro, S., "Passive Smoking and Myocardial Infarction in Women," Abstract, CVD Epidemiology Newsletter No. 43, 29, Winter 1988.

12. Sandler, D.P., Comstock, G.W., Helsing, K.J. and Shore, D.L., "Deaths from All Causes in Non-Smokers Who Lived with Smokers," American Journal of Public Health 79(2): 163-167, 1989.

13. Svendsen, K.H., Kuller, L.H., Martin, M.J. and Ockene, J.K., "Effects of Passive Smoking in the Multiple Risk Factor Intervention Trial," American Journal of Epidemiology 126(5): 783-795, 1987.

14. Wells, A.J., "An Estimate of Adult Mortality in the United States from Passive Smoking," Environment International 14(3): 249-265, 1988.

15. Kawachi, I., Pearce, N.E. and Jackson, R.T., "Deaths from Lung Cancer and Ischaemic Heart Disease Due to Passive Smoking in New Zealand," New Zealand Medical Journal 102(871): 337-340, 1989.

16. Kristensen, T.S., "Cardiovascular Diseases and the Work Environment. A Critical Review of the Epidemiologic Literature on Chemical Factors," Scand. J. Work Environ. Health 15: 245-264, 1989.

17. Glantz, S.A. and Parmley, W.W., "Passive Smoking and Heart Disease: Epidemiology, Physiology, and Biochemistry," Circulation 83(1): 1-12, 1991.

18. U.S. Department of Health and Human Services, The Health Consequences of Involuntary Smoking: A Report of the Surgeon General. Publication No. DHHS (CDC) 87-8398, Washington, D.C., U.S. Government Printing Office, 1986.

19. Committee on Passive Smoking, Board on Environmental Studies and Toxicology, National Research Council, National Academy of Sciences, Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects. Washington, D.C., National

2500061562

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Academy Press, 1986.

20. Wexler, L.M., "Environmental Tobacco Smoke and Cardiovascular Disease: A Critique of the Epidemiological Literature and Recommendations for Future Research." In: Environmental Tobacco Smoke: Proceedings of the International Symposium at McGill University 1989. D.J. Ecobichon and J.M. Wu (eds.). Lexington, Mass., Lexington Books, D.C. Heath and Company, Chapter 8, 139-152, 1990.

21. Weetman, D.F. and Munby, J., "Environmental Tobacco Smoke (ETS) and Cardiovascular Disease." In: Indoor Air Quality and Ventilation. F. Lunau and G.L. Reynolds (eds.). London, Selper Ltd., 211-216, 1990.

22. Thiery, J. and Cremer, P., "Coronary Heart Disease and Involuntary Smoking," Paper presented at: Toxicology Forum (Session on "Environmental Tobacco Smoke: Science and Meta-Science"), Budapest, Hungary, June 19, 1990.

23. Armitage, A.K., "Environmental Tobacco Smoke and Coronary Heart Disease." In: Other People's Tobacco Smoke. A.K. Armitage (ed.). Beverly, E. Yorks, U.K., Galen Press, Chapter 7, 109-116, 1991.

24. McMurray, R.G., Hicks, L.L. and Thompson, D.L., "The Effects of Passive Inhalation of Cigarette Smoke on Exercise Performance," European Journal of Applied Physiology 54(2): 196-200, 1985.

25. Aronow, W.S., "Effect of Passive Smoking on Angina Pectoris," New England Journal of Medicine 299(1): 21-24, 1978.

26. Khalfen, E.Sh. and Klochkov, V.A., "Effect of 'Passive' Smoking on the Physical Load Tolerance of Coronary Heart Disease Patients," Ter. Arkh. 5: 112-115, 1987. [Uncertified translation]

27. Sinzinger, H. and Kefalides, A., "Passive Smoking Severely Decreases Platelet Sensitivity to Antiaggregatory Prostaglandins," Letter, The Lancet II, pp. 392-393, August 14, 1982.

28. Burghuber, O.C., Punzengruber, Ch., Sinzinger, H., Haber, P. and Silberbauer, K., "Platelet Sensitivity to Prostacyclin in Smokers and Non-smokers," Chest 90(1): 34-38, 1986.

29. Sinzinger, H. and Virgolini, I., "Are Passive Smokers at Greater Risk of Thrombosis?" Wiener Klinische Wochenschrift 20: 649-698, 1989.

10381016

2500061563

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

30. Davis, J.W., Shelton, L., Watanabe, I.S. and Arnold, J., "Passive Smoking Affects Endothelium and Platelets," Arach. Intern. Med. 149: 386-389, 1989.

31. Moskowitz, W.B., Mosteller, M., Schiekern, R.M., Bossano, R., Hewitt, J.K., Bodurtha, J.N. and Segrest, J.P., "Lipoprotein and Oxygen Transport Alterations in Passive Smoking Preadolescent Children: The MCV Twin Study," Circulation 81(2): 586-592, 1990.

32. Pomrehn, P., Hollarbush, J., Clarke, W. and Lauer, R., "Children's HDL--chol: The Effects of Tobacco; Smoking, Smokeless and Parental Smoking," Presented at the 30th Annual Conference on Cardiovascular Disease Epidemiology, Abstract, Circulation 81(2): 720, 1990.

33. Gvozdjakova, A., Bada, V., Sany, L., Kucharska, J., Kruty, F., Bozek, P. Trstansky, L. and Gvozdjak, J., "Smoke Cardiomyopathy: Disturbance of Oxidative Processes in Myocardial Mitochondria," Cardiovascular Research 18: 229-232, 1984.

34. Gvozdjakova, A., Kucharska, J., Sany, L., Bada, V., Bozek, P. and Gvozdjak, T., "Effect of Smoking on the Cytochrome and Oxidase System of the Myocardium," Bratisl. lek. Listy 83: 10-15, 1985.

35. Gvozdjak, J., Gvozdjakova, A., Kucharska, J. and Bada, V., "The Effect of Smoking on Myocardial Metabolism," Czech. Med. 10(1): 47-53, 1987.

2500061564

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

PARENTAL SMOKING AND CHILDHOOD RESPIRATORY DISEASE/SYMPTOMS

2500061565

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

PARENTAL SMOKING

Perhaps no claim regarding environmental tobacco smoke (ETS) is as capable of provoking strong feelings as the charge that parents who smoke may compromise the health of their children. While the issue of parental smoking is laden with emotion, the scientific basis for the claim is difficult to interpret. None of the studies that have reported an association between parental smoking and a child's increased risk of developing respiratory infections or symptoms have actually measured exposure to ETS. Virtually all of the studies have failed to control for cross-infections in the home and other important confounding factors. Studies that have controlled for such factors have frequently reported no significant increased risk of respiratory disease in the children of smoking parents.[1-17]

The studies on parental smoking, each with a different sample size, data collection method and analysis, tend to yield factually incompatible and contrary conclusions. For instance, although certain studies and reviews have reported adverse findings,[18-42] others have observed no significant relationship between parental smoking and respiratory illness in children.[5,6,8,43-53] After a five-year study of over 400 children, for example, Dutch researchers concluded there was "no evidence" that parental smoking had an appreciable effect on respiratory symptoms in school children.[49] A similar conclusion was reached by a group of U.S. researchers, including a critic of smoking, who found "no significant relation" between parental smoking and

2500061566

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

respiratory symptoms in a study of nearly 400 families with 816 children in three cities.[43]

In 1988, investigators re-examined thirty studies on ETS exposures among children and evaluated the studies for their scientific validity.[54] They noted that while several studies had reported a statistically significant relationship between ETS exposure and respiratory illness in children, "most studies had significant design problems that prevent reliance on their conclusions." The authors concluded that "many questions remain, and future studies should consider important methodological standards to determine more accurately the effect of passive smoking on child health." In 1990, another group of researchers examined the existing literature on ETS and respiratory health.[55] Although critical of ETS, they concluded that "[f]urther studies of health effects are needed; such studies will require improved methods of exposure assessment, as well as better understanding of dose-response relationships."

The studies on parental smoking have relied solely on questionnaires to obtain exposure data.[55] Reliance on questionnaires casts doubt on the findings of these studies for several reasons. First, it has been noted that even "slight changes" in the way the questions were phrased could result "in substantial differences in the type of responses one obtains."[28] Secondly, one study observed that there was a significant difference in the respiratory symptoms reported depending on which

2500061567

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

parent completed the questionnaire.[38] It has been reported that mothers are more likely than fathers to report chronic respiratory problems in their children and that asymptomatic mothers are less likely than symptomatic mothers to report symptoms in their children.[55] It has been suggested that "[t]hese potential biases must be evaluated in epidemiologic studies."[55]

In conclusion, although a number of studies have been conducted on parental smoking and childhood respiratory health, the results of these studies are inconsistent and are limited by the methodology employed in each study. Questionnaires are not an accurate method of determining the actual exposure of ETS a child receives from his/her smoking parent. Many studies report no relationship for parental smoking, particularly when confounding factors such as diet, home dampness or cross-infection in and outside the home are considered. Childhood respiratory illness appears to be influenced by many different social, familial, and environmental factors. To isolate parental smoking as a cause is scientifically unjustified.

2500061568

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

REFERENCES

1. Anderson, L., et al., "Day Care Center Attendance and Hospitalization for Lower Respiratory Tract Illness," Pediatrics 82(3): 300-308, 1988.

2. Berwick, M., et al., "Lower Respiratory Symptoms in Children Exposed to Nitrogen Dioxide From Unvented Combustion Sources," Environment International 15: 369-373, 1989.

3. Berglund, B., et al., "Radon, Passive Smoking, Particulates and Housing Epidemiology," Indoor Air 2: 255-260, 1984.

4. Brunekreef, B., et al., "Home Dampness and Respiratory Morbidity in Children," Am. Rev. Respir. Dis 140: 1363-1367, 1989.

5. Harrington, W. and Krupnick, Alan J., "Short-Term Nitrogen Dioxide Exposure and Acute Respiratory Disease in Children," JAPCA 35: 1061-1087, 1985.

6. Holma, B. and Winding, O., "Housing, Hygiene, and Health: A Study in Old Residential Areas in Copenhagen," Archives of Environmental Health 32(2): 86-93, 1977.

7. Kerigan, A., et al., "A Three-Year Cohort Study of the Role of Environmental Factors in the Respiratory Health of Children

2500061569

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

in Hamilton, Ontario," Am. Rev. Respir. Dis. 133: 987-993, 1986.

8. Martin, C., et al., "Housing Conditions and Ill Health, " British Medical Journal 294: 1987.

9. Melia, R.J.W., et al., "Association Between Gas Cooking and Respiratory Disease in Children," British Medical Journal, 149-152, 1977.

10. Melia, R.J.W., et al., "The Relation Between Respiratory Illness in Primary Schoolchildren and the Use of Gas for Cooking, I- Results From a National Survey," International Journal of Epidemiology 8(4): 333-338, 1979.

11. National Institutes of Health, Public Health Service, U.S. Department of Health and Human Services, May 1-3, 1983, "Report of Workshop on Respiratory Effects of Involuntary Smoke Exposure: Epidemiologic Studies"

12. Mitchell, E., et al., "Socioeconomic Status in Childhood Asthma," International Journal of Epidemiology 18(4): 888-890, 1989.

13. Nordvall, S.L., et al., "Sensitization of Children in the Stockholm Area to House Dust Mites," Acta Paediatr Scan 77(5): 716-720, 1988.

2500061570

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

14. Osborne, J.S., "Health Effects of Heating With Wood: Chest Illness in Young Children and Indoor Heating with Woodburning Stoves," The Human Equation: Health and Comfort, Indoor Air Quality '89, April 17-20, 1989, San Diego, CA.

15. Platt, S., et al., "Damp Housing, Mould Growth, and Symptomatic Health State," BMJ 298: 1673-1678, 1989.

16. Pope, C., "Respiratory Disease Associated with Community Air Pollution and a Steel Mill, Utah Valley," AJPH 79(5): 623-628, 1989.

17. Strachan, D. and Elton, R., "Relationship Between Respiratory Morbidity in Children and the Home Environment," Family Practice 3(3): 137-142, 1986.

18. Committee on Passive Smoking, Board on Environmental Studies and Toxicology, National Research Council, Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects (Washington: National Academy Press, 1986).

19. U.S. Department of Health and Human Services, The Health Consequences of Involuntary Smoking: A Report of the Surgeon General (U.S. DHHS: Washington, 1986).

2500061571

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

20. Bland, M., et al., "Effect of Children's and Parents' Smoking on Respiratory Symptoms," Arch Dis Child 53(2): 100-105, 1978.

21. Bonham, G. and R. Wilson, "Children's Health in Families with Cigarette Smokers," Am Public Health 71(3): 290-293, 1981.

22. Burchfiel, C., et al., "Passive Smoking in Childhood: Respiratory Conditions and Pulmonary Function in Tecumseh, Michigan," Am Rev Respir Dis 133(6): 966-73, 1986.

23. Cameron, P. and D. Robertson, "Effect on Home Environment Tobacco Smoke on Family Health," J Appl Psychol 57(2): 142-147, 1973.

24. Chen, Y., "Synergistic Effect of Passive Smoking and Artificial Feeding on Hospitalization for Respiratory Illness in Early Childhood," Chest 95: 1004-07, 1989.

25. Colley, J., "Respiratory Symptoms in Children and Parental Smoking and Phlegm Production," Br Med J II: 201-204, 1974.

26. Colley, J., et al., "Influence of Passive Smoking and Parental Phlegm on Pneumonia and Bronchitis in Early Childhood," Lancet II: 1031-1034, 1974.

2500061572

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

27. Dockery, D., et al., "Effects of Inhalable Particles on Respiratory Health of Children," Am Rev Respir Dis 139: 587-594, 1989.

28. Ekwo, E., et al., "Relationship of Parental Smoking and Gas Cooking to Respiratory Disease in Children," Chest 84(6): 662-668, 1983.

29. Fergusson, D., et al., "Parental Smoking and Lower Respiratory Illness in the First Three Years of Life," J Epidemiol Community Health 35(3): 180-184, 1981.

30. Fergusson, D., et al., "Parental Smoking and Respiratory Illness During Early Childhood," Ped Pul 1(2): 99-106, 1985.

31. Ferris, B., et al., "The Six-City Study: Examples of Problems in Analysis of Data," Environ Health Perspect 52: 115-123, 1983.

32. Gortmaker, S., et al., "Parental Smoking and the Risk of Childhood Asthma," Am J Public Health 72(6): 574-579, 1982.

33. Harlap, S. and A. Davies, "Infant Admissions to Hospital and Maternal Smoking," Lancet I: 529-532, 1974.

2500061573

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

34. Kraemer, M., et al., "Risk Factors for Persistent middle Ear Effusions: Otitis Media, Catarrh, Cigarette Smoke Exposure, and Atopy," JAMA 249(8): 1022-1025, 1983.

35. Murray, A., and B. Morrison, "Passive Smoking and the Seasonal Difference of Severity of Asthma in Children," Chest 94(4): 701-708, 1988.

36. Neuspiel, D., et al., "Parental Smoking and Post-Infancy Wheezing in Children: A Prospective Cohort Study," AJPH 79(2): 168-171, 1989.

37. Ogston, S., et al., "Association of Infant Alimentary and Respiratory Illness with Parental Smoking and Other Environmental Factors," J Epidemiol Commun Health 41(1): 21-25, 1987.

38. Schenker, M., et al., "Risk Factors for Childhood Respiratory Disease: The Effect of Host Factors and Home Environmental Exposures," Am Rev Respir Dis 128: 1038-1043, 1983.

39. Somerville, S., et al., "Passive Smoking and Respiratory Conditions in Primary School Children," J Epidemiol Commun Health 42(2): 105-110, 1988.

2500061574

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

40. Strachan, D., et al., "Passive Smoking, Salivary Cotinine Concentrations, and Middle Ear Effusion in 7 Year Old Children," BMJ 298: 1549-1552, 1989.

41. Tsimoyianis, G., et al., "Reduction in Pulmonary Function and Increased Frequency of Cough Associated With Passive Smoking in Teenage Athletes," Pediatrics 80(1): 32-36, 1987.

42. Ware, J., et al., "Passive Smoking, Gas Cooking, and Respiratory Health of Children Living in Six Cities," Am Rev Respir Dis 129: 366-374, 1984.

43. Schilling, R., et al., "Lung Function, Respiratory Disease, and Smoking in Families," Am J Epidemiol 106(4): 274-283, 1977.

44. Camacho, E., et al., "Pulmonary Symptoms and Pulmonary Functional Tests Among Children in Relation to the Area of Residence," Eur Respir Dis 63(2): 165-166, 1982.

45. Binder, R., et al., "Importance of the Indoor Environment in Air Pollution Exposure," Arch Environ Health 31(6): 277-279, 1976.

46. Bouhuys, A., "Lung Diseases in Rural and Urban Communities," Report Sponsored by the Division of Lung Diseases, National

2500061575

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Heart, Lung and Blood Institute, U.S. National Institutes of Health, pp. 77-89, June 10, 1977.

47. Gardner, G., et al., "Effects of Social and Family Factors on Viral Respiratory Infection and Illness in the First Year of Life," J Epidemiol Community Health 38: 42-48, 1984.

48. Kallail, K., et al., "Passive Smoking and Middle Ear Problems in Kansas Public School Children," J Commun Disord 20: 187-96, 1987.

49. Kerrebijn, J., et al., "Chronic Nonspecific Respiratory Disease in Children, A Five Year Follow-Up Study," Acta Paediatr Scand, Suppl. 261: 11-72, 1977.

50. Lebowitz, M. and B. Burrows, "Respiratory Symptoms Related to Smoking Habits of Family Adults," Chest 69(1): 48-50, 1976.

51. Love, G., et al., "The Incidence and Severity of Acute Respiratory Illness in Families Exposed to Different Levels of Air Pollution, New York Metropolitan Area, 1971-72," Arch Environ Health 36(2): 66-73, 1981.

52. Salzman, M., et al., "Passive Smoking and Croup," Arch Otolaryngol Head Neck Surg 113: 866-868, 1987.

2500061576

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

53. Shy, C., et al., "The Chattanooga School Children Study: Effects of Community Exposure to Nitrogen Dioxide. II. Incidence of Acute Respiratory Illness," J Air Pollut Control Assoc 20(9): 582-588, 1970.

54. Rubin, D. and K. Damus, "The Relationship Between Passive Smoking and Child Health: Methodologic Criteria Applied to Prior Studies," Yale J Bio Med 61(5): 401-411, 1988.

55. Schenker, M.B. and Pocekay, D.E., "Environmental Tobaco Smoke: Assessment of Exposure and Effects on Respiratory Health" Problems in Resp. Care 3(2): 193-205, 1990.

2500061577

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

PARENTAL SMOKING AND CHILDRENS' LUNG FUNCTION

2500061578

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

LUNG FUNCTION IN CHILDREN

The studies that have investigated lung function in children and its possible relationship to environmental tobacco smoke exposure are presented in this section. To aid in the interpretation of this literature, definitions of the major lung function parameters are provided below.

Df: One of the most widely used measures of pulmonary function in adults and children is forced vital capacity and is represented in the literature as FVC. This term refers to the maximum volume of gas that a person can expire as forcefully and rapidly as possible from their lungs immediately following a maximal inspiration of air. When a person's ability to expire air forcefully and rapidly from their lungs (FVC) is compromised, this can possibly be an indication of chronic obstructive lung disease. Decreased FVC is common in restrictive diseases such as pulmonary fibrosis and in obstructive diseases such as emphysema and asthma.

Df: A second important measure of pulmonary function is the forced expiratory volume in one second, which is abbreviated as FEV1 in the literature. The FEV1 measure is simply the amount of air that is expired in the first second of the FVC maneuver. As with FVC, this parameter is useful in the assessment of airway obstruction. The two parameters, FVC and FEV1, are often used in a ratio to determine the percentage of a person's FVC that is expired in the first second of the maneuver. A FEV1/FVC ratio lower than 65% to 70% is characteristic of obstructive lung disease. On the other hand, subjects with restrictive lung disease will often show a normal or exaggerated FEV1/FVC value.

Df: Forced expiratory flow, known as FEF25%-75%, is the average rate of flow of air during the middle half of an FEV maneuver. The FEF25%-75% is indicative of the status of the medium and small sized airways. Decreased values of FEF25%-75% are common in the early stages of obstructive lung disease. Low values of FEF25%-75% in combination with normal values of FVC and FEV1 are often indicative of early small airways abnormality. Reduced FEF25%-75% are sometimes seen in cases of severe restrictive disease as well.

All of these measures share a common problem: accurate assessment requires the full cooperation and maximal effort of the subjects under investigation. Accurate measures are sometimes

2500061579

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

therefore difficult to obtain, especially when the subjects are young children who do not fully comprehend the requirements being made of them in the pulmonary function tests. The studies are not consistent in the lung function parameters they measure, and there is also a lack of consistency among the results of the same function tests across studies. Following is a presentation of the major studies that have examined these lung function parameters in children. The investigators who have found associations between impaired lung function and ETS exposure are often uncertain of the clinical meanings of the small decreases observed in their studies. Therefore, it is not suprising that no definitive conclusions have been reached regarding ETS exposure and its possible association with lung function in children.

2500061580

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

REFERENCE

Ruppel, Gregg. Manual of pulmonary function testing (Fourth edition). The C.V. Mosby Company, 1986, pp. 33-38.

2500061581

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

RESULTS OF SELECTED STUDIES: CHILDHOOD LUNG FUNCTION

STUDY	EFFECT ON FEV1, FEV.75	EFFECT ON FEF25-75%
Tager 1976	decrease	not reported
Tager 1979	none	decrease
Weiss 1980	none	decrease
Tager 1983	decrease 7%	none
O'Connor 1987	decrease 5-7%	decrease 14-15%
Ware 1984	decrease .6-.9%	not reported
Berkey 1986	decrease .85%	not reported
Hasselblad 1981	decrease .5-2%	not reported
Tashkin 1984	none	decrease 2.5%
Ekwo 1983	none	none
Vedal 1984	none	decrease 4%
Spinaci 1985	decrease	none
Chen 1986	decrease 3%	decrease 6%
Burchfiel 1986	decrease 4-5%	not reported
Yarnell 1979	decrease 3%	decrease 12%
Teculesco 1986	decrease 5%	not reported
Tsimoyianis 1987	not done	decrease
Lebowitz 1987	none	not done
Leeder 1976	not done	not done
Schilling 1977	none	not reported
Speizer 1980	none	not reported
Dodge 1982	none	not reported
Lebowitz 1984	none	not reported
Lebowitz 1984	not done	not done

Adapted from Witorsch 1989

2500061582

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

PARENTAL SMOKING AND COMPROMISED CHILDREN

2500061583

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

COMPROMISED CHILDREN

The literature on environmental tobacco smoke includes a body of research on asthma and the relationship between parental smoking and preexistent disease in children. While only a few studies have been conducted thus far on children with, for example, cystic fibrosis (a genetic disorder whereby lung passages often become blocked by abnormally behaving mucus), there have been numerous studies that have examined asthmatic children and the presence of smokers in the home. The results of the studies have been variable and are subject to the influences of many different confounders such as socioeconomic status, genetic determinants, damp housing, and gas cooking in the home. It is not suprising, therefore, that researchers are inconsistent in their interpretation of the available data on exposure to ETS and childhood asthma. Following is a presentation of the major studies that have examined a possible association of ETS with asthma in children. Also included are the studies available on children with cystic fibrosis.

2500061584

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

RESULTS OF SELECTED STUDIES: COMPROMISED CHILDREN

Leeder, et al., 1976	Reported that episodes of asthma in the first five years of life showed an association with parental history of asthma-wheeze and that there is little relationship between asthma in the first five years of life and other family, social, or environmental factors.
Fergusson, et al., 1985	Reported that maternal smoking increased the risk of lower respiratory infections/symptoms during the child's first two years of life, and that after two years this association seemed to disappear. Also reported that there was no increased risk of asthma or asthma attacks attributable to maternal smoking.
Horwood, et al., 1985	Reported that there was no evidence to suggest that the structure, practices (including parental smoking), or the dynamics of the family played a significant role in the development of childhood asthma.
Murray, et al., 1986	Reported that maternal smoking aggravated symptoms in asthmatic children.

2500061585

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Anderson, et al., 1987	Reported that sex of child, mother's age at the child's birth, pneumonia, whooping cough, tonsillectomy, adenoidectomy, allergic rhinitis, eczema and periodic abdominal pain/vomiting attacks were associated with the development of childhood asthma.
Evans, et al., 1987	Reported that parental smoking increased the number of emergency room visits of children with asthma. The lack of an association between parental smoking and symptoms in asthmatic children caused the authors to question the mechanism whereby parental smoking would increase ER visits.
Toyoshima, et al., 1987	Reported that it was not clear whether parental smoking increased the incidence of asthmatic disease in children.
Kershaw, 1987	The authors conceded that the association observed with parental smoking may reflect a relationship of smoking behaviour to a number of other social factors such as medical care utilization and maternal stress.
Murray, et al., 1988	Reported that paternal smoking, including the number of cigarettes the father smoked at home, had no association with any test results. Maternal smoking in the "wet and cold" season was reported to increase the severity of the child's asthma. There was no assocation in the "warm and dry" season

2500061586

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

	and the severity of the child's asthma. The authors attribute this to increased ventilation in the "warm and dry" season.
Somerville, et al., 1988	Reported a positive association between parental smoking and asthma in girls and a non-significant negative relation between parental smoking and asthma in boys.
Oldigs, et al., 1990	Reported that in children with mild bronchial asthma one hour of passive smoke exposure did not cause airway obstruction or changes in bronchial responsiveness.
Sherman, et al., 1990	Neither bronchiolitis, eczema, croup, personal cigarette smoking, maternal smoking, paternal smoking, nor delivery complications bore an apparent relation to the development of childhood asthma.
Weitzman, et al., 1990	The authors concede that the estimate of children's exposure to cigarette smoke is "crude", based on parent reporting of smoking during pregnancy.
Rubin, 1990	Reported an association between parental smoking and the severity of cystic fibrosis in children. However, the authors conceded that it could not be ruled out that social, economic, or other factors determined both the smoking status of the household and the nutritional status of the children.

2500061587

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Gilljam, et al., 1990	Reported that there was no statistical difference in clinical status or pulmonary function between children with cystic fibrosis from smoking and nonsmoking families. For patients with higher levels of physical activity, parental smoking appeared to matter less.
Young, et al., 1991	Reported that parental smoking may contribute to a higher level of airway responsiveness early in the child's life. The authors conceded that they did not report the actual amount of parental smoking due to the inaccuracies of parental reporting.

2500061588

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

PARENTAL SMOKING AND OTITIS MEDIA IN CHILDREN

2500061589

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

OTITIS MEDIA ("GLUE EAR")

In addition to claims that parental smoking affects the respiratory health of children, there are claims that exposure to parental smoking might increase the risk of otitis media (commonly known as "glue ear") in children. Otitis media is an inflammation of the inner ear that often leads to an accumulation of fluid in the inner ear canal. Otitis media often appears as a complication of various viral and bacterial infections, including measles. If left undetected, otitis media can lead to hearing loss and learning disabilities. Authors of studies examining this issue have not formulated a widely accepted mechanism for how ETS might increase the risk of otitis media in children. There are two theories that are proposed but have not been scientifically proven: 1) One theory is that ETS somehow chronically irritates the eustachian tube of the inner ear, leading to the inflammation; and 2) The second theory is that ETS potentially increases the risk of upper respiratory tract infections that spread to the inner ear. The results of the studies on this subject are variable and are subject to the same confounders that potentially bias the results of studies on other ETS related issues. While the science on this issue is controversial, the reported seriousness of otitis media makes investigators anxious to make recommendations for child safety. However, the studies on otitis media and parental smoking have not established a clear association.

2500061590

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

RESULTS OF SELECTED STUDIES ON OTITIS MEDIA

Said, et al., 1978	Reported that number of tonsillectomies/adenoidectomies were related to the amount of parental smoking in the home
Pukander, et al., 1985	Reported that parental smoking in the home increased the risk of acute otitis media and that breast-feeding seemed to have a protective effect
Kallail, et al., 1987	Reported that parental smoking was not associated with the occurrence of otitis media
Zielhuis, 1989	Reported that parental smoking was not related to an increased risk of otitis media
Strachan, 1990	Reported that parental smoking was an important determinant of middle-ear underpressure and effusion
Strachan, 1989	Reported that approximately one-third of the cases of middle ear effusion in their subjects were attributable to passive smoking
Taninio, et al., 1988	Reported that parental smoking was more prevalent among the subjects with recurrent otitis media
Kraemer et al, 1983	Reported that parental smoking, atopy, and catarrh posed the greatest risk to children of developing persistent middle-ear effusions when present together in the same child

2500061591

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Pukander, et al., 1990	Reported that maternal smoking increased the risk of acute otitis media in infants and especially of recurrent attacks
Vinther, et al., 1982	Reported that there were no effects of parental smoking on the frequency of otitis media in children
Moorhead, 1985	Reported that otitis media was found to be related to parental smoking in this general practice study
Black, 1985	Reported that parental smoking increased a child's risk of undergoing surgery for otitis media
Fleming, et al., 1987	Reported that full time day-care attendance increased the risk of ear infections (odds ratio = 3.8)

2500061592

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

ETS AND ADULT RESPIRATORY DISEASE/SYMPTOMS

2500061593

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

ADULT RESPIRATORY DISEASE

Several studies have examined respiratory disease and symptoms and their possible association with exposure to environmental tobacco smoke in adults. The studies that examined respiratory disease and symptoms in adults are contained in this section. For additional studies on adults, see the "compromised individuals" and "lung function" sections.

2500061594

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

RESULTS OF SELECTED STUDIES: ETS AND ADULT RESPIRATORY HEALTH

Lee, 1986	Passive smoking was not associated with an increased risk of chronic bronchitis in the nonsmoker.
Koo, et al., 1988	Reported an association between respiratory symptoms in the mothers and the same symptoms in their children. Indicates that cross-infection is an important confounder of studies on parental smoking and childhood respiratory health.
Hole, et al., 1989	Reported an association between passive smoking and adverse cardiorespiratory symptoms in adult nonsmokers. None of the associations, however, were significant.
Koo, et al., 1990	With the exception of smoking by the father and the children's NO2 levels, no association was found between smoking at home and NO2 levels.

2500061595

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

ETS AND ADULT LUNG FUNCTION

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

2500061596

LUNG FUNCTION IN ADULTS

The studies that have investigated lung function in adults and its possible relationship to environmental tobacco smoke exposure are presented in this section. To aid in the interpretation of this literature, definitions of the major lung function parameters are provided below.

Df: One of the most widely used measures of pulmonary function in adults and children is **forced vital capacity** and is represented in the literature as **FVC**. This term refers to the maximum volume of gas that a person can expire as forcefully and rapidly as possible from their lungs immediately following a maximal inspiration of air. When a person's ability to expire air forcefully and rapidly from their lungs (FVC) is compromised, this can possibly be an indication of chronic obstructive lung disease. Decreased FVC is common in restrictive diseases such as pulmonary fibrosis and in obstructive diseases such as emphysema and asthma.

Df: A second important measure of pulmonary function is the **forced expiratory volume in one second**, which is abbreviated as **FEV1** in the literature. The FEV1 measure is simply the amount of air that is expired in the first second of the FVC maneuver. As with FVC, this parameter is useful in the assessment of airway obstruction. The two parameters, FVC and FEV1, are often used in a ratio to determine the percentage of a person's FVC that is expired in the first second of the maneuver. A **FEV1/FVC ratio** lower than 65% to 70% is characteristic of obstructive lung disease. On the other hand, subjects with restrictive lung disease will often show a normal or exaggerated FEV1/FVC value.

Df: **Forced expiratory flow**, known as **FEF25%-75%**, is the average rate of flow of air during the middle half of an FEV maneuver. The FEF25%-75% is indicative of the status of the medium and small sized airways. Decreased values of FEF25%-75% are common in the early stages of obstructive lung disease. Low values of FEF25%-75% in combination with normal values of FVC and FEV1 are often indicative of early small airways abnormality. Reduced FEF25%-75% are sometimes seen in cases of severe restrictive disease as well.

All of these measures share a common problem: accurate assessment requires the full cooperation and maximal effort of the subjects under investigation. Accurate measures are sometimes

2500061597

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

therefore difficult to obtain. The studies are not consistent in the lung function parameters they measure, and there is also a lack of consistency among the results of the same function tests across studies. Following is a presentation of the major studies that have examined these lung function parameters in adults. The investigators who have found associations between impaired lung function and ETS exposure are often uncertain of the clinical meanings of the small decreases observed in their studies. Therefore, it is not suprising that no definitive conclusions have been reached regarding ETS exposure and its possible association with lung function in adults.

2500061598

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

REFERENCE

Ruppel, Gregg. Manual of pulmonary function testing (Fourth edition). The C.V. Mosby Company, 1986, pp. 33-38.

2500061599

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

RESULTS OF SELECTED STUDIES: ETS AND ADULT LUNG FUNCTION

Bouhuys, et al., 1978	The authors reported no associations between smoking in the home and increased symptoms or lung function loss among nonsmokers living in the same households.
Shephard, et al., 1979	The authors raise the possibility that subjective reporting of symptoms could have been "suggested" by the odor of the cigarette smoke.
White, et al., 1980	This study has received numerous criticisms.
Comstock, et al., 1981	Passive smoking in the home was not associated with the prevalence of respiratory symptoms and was only "suggestively associated" with impaired ventilatory function.
Kauffmann, et al., 1983	Opposite trends in FEV1 and FEF25-75 were found in men passively exposed to tobacco smoke, and the differences observed in women were slight and not statistically significant.
Jones, et al., 1983	The use of cooking fuels was found to be associated with impaired ventilatory function in a group of nonsmoking women.
Kentner, et al., 1984	Passive inhalation of tobacco smoke at home or the workplace was found not to be associated with impaired lung function in healthy nonsmokers.
Lebowitz, et al., 1985	Reported no direct association between ETS and lung function parameters in adult nonsmokers.

2500061600

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Hosein, et al., 1986	The use of gas stoves was found to be associated with impaired lung function in women. It was reported that passive smoking in households where gas stoves were used appeared to have no effect on lung function values.
Masi, et al., 1988	The authors concede that their use of multiple tests of significance (involving both exposure and response measurements) are likely to have resulted in some associations achieving statistical significance by chance.
Kalandidi, et al., 1990	Assessment of exposure was based solely on the husband's smoking habit in terms of amount (daily), amount (total), and duration.

2500061601

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

ETS AND COMPROMISED ADULTS

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

2500061602

COMPROMISED ADULTS

The literature on environmental tobacco smoke includes a body of research on asthmatic adults. Studies have been conducted in order to attempt to determine whether there is a relationship between passive exposure to ETS and the development of asthma or the exacerbation of existing asthma in adults. The studies are varied in their results, and accordingly, no definitive conclusions have been reached by investigators. Following are the studies that examine ETS and its possible relation to asthma in adults.

2500061603

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

COMMENTS ON SELECTED STUDIES: ETS AND COMPROMISED ADULTS

Stahle, et al., 1978	The authors suggest that tobacco smoke exposure might trigger asthma attacks by means of an allergic reaction.
Shephard, et al., 1979	Reported that asthmatic subjects did not appear to have an unusual sensitivity to tobacco smoke exposure.
Dahms, et al., 1981	Five of the ten subjects specifically reported sensitivity to tobacco smoke before their inclusion in this study.
Ing, et al., 1983	This study investigated only six subjects.
Romer, et al., 1983	The authors concede that the small subject population of this study indicates that the results must be taken with caution.
Knight, et al., 1985	Only six subjects were studied.
Wiedemann, et al., 1986	The authors report that passive smoking presents no acute respiratory risk to young asymptomatic asthmatic patients.
Stankus, et al., 1988	Only 21 subjects were included and all had complained of respiratory symptoms upon previous exposure to environmental tobacco smoke.
Bailey, et al., 1990	No relationship was observed between passive smoking and pulmonary function of asthmatic subjects.

2500061604

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

CONFOUNDERS

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

CONFOUNDERS

Studies on parental smoking and childhood respiratory disease rarely address confounding variables. Confounding variables are factors that can create a "false" association between two elements by being associated with one or both of them. For example, factor X (socioeconomic status) may be associated with both factor Y (parental smoking) and factor Z (childhood respiratory disease). When factor X is not controlled for in epidemiological studies of the possible association between factor Y and factor Z, a false association may appear between factors Y and Z. Therefore, it is vital that epidemiologists control for confounding variables when conducting studies such as those on parental smoking. The possible confounding variables associated with parental smoking and childhood respiratory disease can be grouped into four major categories: (1) household heating and cooking sources; (2) outdoor air pollution; (3) organic substances; and (4) demographic, medical and socioeconomic factors.

2500061606

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Household heating and cooking sources

Children living in households with gas stoves have been reported to have a greater history of respiratory illness before the age of two and small but significantly lower levels of FEV_1 and FVC corrected for height[1] (FEV1 and FVC are standard measurements of lung capacity and function). Similarly, exposure of children to gas cooking in the first two years of life has been associated with an increased risk of hospitalization for respiratory illness[2]. There are reported associations of gas stove use with daily peak flow in asthmatic, normal, and allergic subjects.[3]

Oxides of nitrogen (NOx) arising from the use of gas stoves for cooking were proposed to be related to a reported increase in cough, "colds going to the chest," and bronchitis in a study of 5,758 English and Scottish children aged six to eleven years[4]. A number of other confounders were controlled for in this study, including "age, social class, latitude, population density, family size, overcrowding, outdoor levels of smoke and sulphur dioxide and types of fuel used for heating." One group of researchers reported similar results for a five-year longitudinal study of 4827 boys and girls, ages five to ten years. This reported association was independent of age, sex, social class, number of cigarette smokers in the home, and latitude, and was only found in urban areas.[5]

2500061607

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Use of unvented kerosene heaters, which release nitrogen dioxide (NO_2) into the indoor environment, was associated with significantly more days of acute respiratory illness in exposed children[6]. In this study, there was no difference in the number of cigarettes smoked daily in the homes of exposed versus unexposed children. NO_2 exposure was also reported to be associated with a risk of reporting lower respiratory symptoms in children under the age of seven[7].

One study reported increased proportions of chest illnesses and hospitalizations for chest illness before age two in young children living in homes heated by wood-burning stoves. Medical histories, sociodemographic factors, or exposure to other pollutant sources did not account for the reported association[8].

In another report, hot water heating systems were reported to have a large effect on lung function in children, when compared to the use of forced air heating and air conditioning systems[9].

2500061608

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

REFERENCES

1. Speizer, F., et al., "Respiratory Disease Rates and Pulmonary Function in Children Associated with NO_2 Exposure," American Review of Respiratory Disease, 121(1): 3-10, 1980.

2. Ekwo, E.E., et al., "Relationship of Parental Smoking and Gas Cooking to Respiratory Disease in Children," Chest 84(6): 662-668.

3. Lebowitz, M.D., "The Effects of Environmental Tobacco Smoke Exposure and Gas Stoves on Daily Peak Flow Rates in Asthmatic and Non-Asthmatic Families," ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels, eds., R. Rylander, et al., European Journal of Respiratory Diseases Suppl., 133(65): 90-97, 1984.

4. Melia, R.J.W., et al., "Association Between Gas Cooking and Respiratory Disease in Children," British Medical Journal, 149-152, 1977.

5. Melia, R.J.W., et al., "The Relation Between Respiratory Illness in Primary Schoolchildren and the Use of Gas for Cooking, I - Results From a National Survey," International Journal of Epidemiology, 8(4): 333-338, 1979.

2500061609

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

6. Berglund, B., et al., "Radon, Passive Smoking, Particulates and Housing Epidemiology," Indoor Air 2: 255-260, 1984.

7. Berwick, M., et al., "Lower Respiratory Symptoms in Children Exposed to Nitrogen Dioxide From Unvented Combustion Sources," Environment International 15: 369-373, 1989.

8. Osborne, J.S. and R.E. Honicky, "Health Effects of Heating With Wood: Chest Illness in Young Children and Indoor Heating with Woodburning Stoves," The Human Equation: Health and Comfort, ASHRAE/SOEH Indoor Air Quality '89, April 17-20, 1989, San Diego, CA.

9. Hosein, H.R., et al., "The Effect of Domestic Factors on Respiratory Symptoms and FEV_1," International Journal of Epidemiology 18(2): 390-396, 1987.

2500061610

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Outdoor air pollution

Outdoor air pollutants have been identified as a confounder in several studies. In one study, acute respiratory disease incidence was reported to be positively associated with higher ambient sulfate levels[1].

A group of researchers examined the importance of indoor and outdoor environmental factors (parental smoking, gas cooking, suspended particulates and sulfur dioxide) in the respiratory health of seven- to ten-year-old Canadian children. The researchers were unable to identify any effects of parental smoking or gas cooking because the prevalence of these variables was highest in an industrial area of high particulate pollution[2].

One researcher has reported a strong association between respiratory illness and particulate pollution in children living in a study site which experiences relatively high levels of particulate pollution[3].

A study comparing Israeli children living in a polluted industrial town versus those living in an unpolluted area reported that chronic respiratory symptoms and most pulmonary diseases were significantly more common among those children from the polluted town[4].

2500061611

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

REFERENCES

1. Harrington, W. and Krupnick, Alan J., "Short-Term Nitrogen Dioxide Exposure and Acute Respiratory Disease in Children," JAPCA 35: 1061-1087, 1985.

2. Kerigan, A., et al., "A Three-Year Cohort Study of the Role of Environmental Factors in the Respiratory Health of children in Hamilton, Ontario," American Review of Respiratory Disease, 133: 987-993, 1986.

3. Pope, C., "Respiratory Disease Associated with Community Air Pollution and a Steel Mill, Utah Valley," AJPH, 79(5): 623-628, 1989.

4. Goren, A.I. and S. Hellmann, "Prevalence of Respiratory Symptoms and Diseases in Schoolchildren Living in a Polluted and in a Low Polluted Area in Israel," Environmental Research 45: 28-37, 1987.

2500061612

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Organic substances

The relevance of home dampness in the etiology of respiratory symptoms in children is supported by current research which links dampness with the presence of molds, dust mites, fungi and other allergenic microbes.

In one study, odds ratios of 1.23 and 2.16 were reported for home dampness after adjustment for several factors, including maternal smoking, in a cohort study of 4,625 eight- to twelve-year-old children living in six United States cities[1]. The authors reported odds ratios for molds of 1.27 to 2.12 after adjustment for maternal smoking and several other factors.

Another study reported higher rates of respiratory symptoms and symptoms of infection and stress among children living in damp houses. The presence of "fungal mould" was also reported to be related to higher rates of respiratory symptoms, independent of smoking in the household[2]. In another study, the growth of fungi and molds in the home was directly related to respiratory symptoms and sensitization to common allergens in children[3].

Researchers have reported that children living in damp and moldy dwellings had a greater prevalence of respiratory symptoms and headache and fever than those living in dry homes. The authors reported a dose-response relationship with increasing

2500061613

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

numbers of symptoms reported in dwellings with higher severity of dampness and mold. All these differences persisted after controlling for possible confounding factors such as household income, cigarette smoking, unemployment, and overcrowding[4].

Atopic sensitization of children to house dust mites was reported to be related to home dampness[5].

2500061614

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

REFERENCES

1. Brunekreef, B., et al., "Home Dampness and Respiratory Morbidity in Children," American Review of Respiratory Diseases 140: 1363-1367, 1989.

2. Martin, C., et al., "Housing Conditions and Ill Health," British Medical Journal, 294: 1987.

3. Ownby, D. and J. McCullough, "Passive Exposure to Cigarette Smoke Does Not Increase Allergic Sensitization in Children," J Allergy Clin Immunol 82(4): 634-638, 1988.

4. Platt, S., et al., "Damp Housing, Mould Growth, and Symptomatic Health State," British Medical Journal, 298: 1673-1678, 1989.

5. Nordvall, S.L., et al., "Sensitization of Children in the Stockholm Area to House Dust Mites," Acta Paediatr Scan, 77(5): 716-720, 1988.

2500061615

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Demographic, medical and socioeconomic factors

Low socioeconomic status has been associated with an increased incidence of respiratory complications[1]. Factors related to lower socioeconomic status include: inadequate medical care, poor nutrition, poor outdoor air quality, increased parental coughing, higher gas stove usage, frequent change of address, and lower per capita living space. In a study of 1,050 European children aged eight and nine years, lifetime and current prevalence of wheeze were both significantly higher in children from low socioeconomic status[2].

Watkins, et al., (1986) reported high consultation rates for respiratory illness in children whose fathers were in manual occupations. This association was not explained by crowded home conditions or parental smoking[3]. Gardner, et al., (1984) reported significantly higher rates of lower respiratory disease in infants of low socioeconomic status[4].

Cross-infection also plays a role in the incidence of children's respiratory disease. For instance, in a 1988 paper, Koo, et al., reported that among Japanese and Hong Kong Chinese women, there was a highly significant correlation between the frequency of maternal respiratory illness and the frequency of respiratory illness in her children[5].

2500061616

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Cross-infection may be relevant to the reports of associations between day care attendance and respiratory illness. Anderson, et al., (1988) reported that care outside the home (day care) is an important factor for acquiring lower respiratory tract illness and infectious diseases in children under two years of age[6]. Gardner, et al., (1984) also noted significantly higher rates of lower respiratory disease among day care infants[4]. Fleming, et al., (1987) reported an increased risk for upper respiratory tract infection associated with day care attendance[7].

Familial characteristics and genetics may also act as confounders. For instance, in a 1982 publication, Lebowitz, et al., report that an observed relationship between children's pulmonary function and parental smoking disappeared when household aggregation of body mass was taken into account[8]. Another Lebowitz, et al., study (1984) also reported that there was "no remaining independent aggregation of pulmonary function measurements" after familial aggregation of body habitus was controlled for[9]. Genetic predisposition may play a role in respiratory illness and pulmonary function[10]; although cross-infection is also involved[11].

"Lifestyle" may also act as a confounder. A study in Copenhagen (Holma and Winding, 1977) examined 109 social, medical, housing, and hygiene factors on morbidity. The best predictors for health were "thriving" (satisfaction), followed by "housing standard" and "personal hygiene." The authors reported no effect

2500061617

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

of parental cigarette smoking on the respiratory health of young children[12]. A survey of 314 nonsmoking Hong Kong Chinese women and their children and 243 Japanese women and their children reported that chronic cough and sputum symptoms were at least 10 times more prevalent in Hong Kong[5]. This observation was attributed to occupational exposure to dust or fumes and household crowding among the Hong Kong mothers.

2500061618

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

REFERENCES

1. Kerigan, A., et al., "A Three-Year Cohort Study of the Role of Environmental Factors in the Respiratory Health of Children in Hamilton, Ontario," American Review of Respiratory Diseases, 133: 987-993, 1986.

2. Mitchell, E., et al., "Socioeconomic Status in Childhood Asthma," International Journal of Epidemiology, 18(4): 888-890, 1989.

3. Watkins, C.J., et al., "Patterns of Respiratory Illness in the First Year of Life," British Medical Journal, 293: 794-796, 1986.

4. Gardner, G., et al., "Effects of Social and Family Factors on Viral Respiratory Infection and Illness in the First Year of Life," Journal of Epidemiology and Community Health 38(1): 42-48, 1984.

5. Koo, L., et al., "A Comparison of the Prevalence of Respiratory Illness Among Nonsmoking Mothers and Their Children in Japan and Hong Kong," Respiratory Illnesses Among Japanese and Chinese Mothers and Their Children: 290-295, 1988.

2500061619

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

6. Anderson, L., et al., "Day Care Center Attendance and Hospitalization for Lower Respiratory Tract Illness," Pediatrics 82(3): 300-308, 1988.

7. Fleming, D.W., et al., "Childhood Upper Respiratory Tract infections: To What Degree Is Incidence Affected by Day-Care Attendance?" Pediatrics 79(1): 55-60, 1987.

8. Lebowitz, M., et al., "The Effect of Passive Smoking on Pulmonary Function in Children," Environment International, 8: 371-373, 1982.

9. Lebowitz, M., et al., "Family Aggregation of Pulmonary Function Measurements," American Review of Respiratory Diseases, 129: 8-11, 1984.

10. Colley, J.R.T., et al., "Influence of Passive Smoking and Parental Phlegm on Pneumonia and Bronchitis in Early Childhood," The Lancet II: 1031-1034, 1974.

11. Colley, J.R.T., "Respiratory Symptoms in Children and Parental Smoking and Phlegm Production," British Medical Journal 2: 201-204, 1974.

2500061620

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

12. Holma, B. and Winding, O., "Housing, Hygiene, and Health: A Study in Old Residential Areas in Copenhagen," Archives of Environmental Health 32(2): 86-93, 1977.

2500061621

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

PARENTAL SMOKING: CONFOUNDING VARIABLES

Access to medical care

Age of mother

Air pollution

Birth weight

Breast feeding

Cooking practices/type

Day care attendance

Diet

Family history of illness

Family size

Gender of child

Genetic determinants

Heating type

Home dampness

Hospital spread of illness

Household pets

Newborn illnesses

Nurture

Overcrowding

Parental education

Parental infections

Place of residence

Seasonal variation

Skin test reactivity (allergy)

Socioeconomic status

2500061622

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

I. HEALTH CLAIMS

- The claim that exposure to environmental tobacco smoke (ETS) in the workplace causes disease in nonsmokers is not justified on a scientific basis.

Exposure

- Measurements taken in offices, workplaces and public places indicate that the contribution of tobacco smoke to indoor air is minimal.[1] For example, typical nicotine measurements (which are particularly revealing because nicotine is unique to tobacco smoke) range from an exposure equivalent of 1/100 to 1/1000 of one filter cigarette per hour.[2] In other words, a nonsmoker would have to spend from 100 to 1000 hours in an office, restaurant or public place in order to be exposed to the nicotine equivalent of just one cigarette.

Lung Function

- A 1980 report[3] which concluded that nonsmokers exposed to tobacco smoke at work for 20 or more years had reduced function of the small airways compared to nonsmokers not so exposed still receives considerable attention, although it was heavily criticized for questionable data acquisition and analysis.[4] In contrast, a more recent study of 1,351 German office workers reportedly found "no evidence" that everyday exposure to

2500061623

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

tobacco smoke in the office or at home leads to an essential reduction of lung function in healthy adults.[5]

Lung Cancer

- Nine of the published studies on spousal smoking and lung cancer examined workplace exposure to ETS and the incidence of lung cancer in nonsmokers.[6] Not one of the studies provides adequate support for an association between ETS exposure in the workplace and lung cancer.

Allergy

- One of the most widespread beliefs, especially in the workplace setting, is that some nonsmokers are "allergic" to tobacco smoke. Scientific researchers, however, have not identified specific allergens in tobacco smoke.[7] Thus, while some individuals may react to the sight or smell of tobacco smoke, this does not mean that they are experiencing an "allergic" reaction to it.

2500061624

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

REFERENCES

1. Kirk, P., et al., "Environmental Tobacco Smoke in Indoor Air," Indoor and Ambient Air Quality, eds. R. Perry and P. Kirk, London, Selper Ltd.: 99-112, 1988.

Sterling, T., et al., "Environmental Tobacco Smoke and Indoor Air Quality in Modern Office Work Environment," J. of Occup. Med. 29(1): 57-62, 1987.

Proctor, C., et al., "Measurement of Environmental Tobacco Smoke in an Air-Conditioned Office Building," Present and Future of Indoor Air Quality, eds. C. Bieva et al., Amsterdam, Elsevier Science Publishers: 169-172, 1989.

Crawford, W., "Health Effects of Passive Smoking in the Workplace," Indoor and Ambient Air Quality, eds. R. Perry and P. Kirk, London, Selper Ltd.: 203-210, 1988.

Oldaker, G., et al., "Results from Surveys of Environmental Tobacco Smoke in Offices and Restaurants," Indoor Air Quality, ed. H. Kasuga, Springer-Verlag, Berlin Heidelberg: 99-104, 1990.

2. Badre, R., et al., "Pollution Atmospherique par la Fumee de Tabac (Atmospheric Pollution by Smoking)," Ann. Pharm. Fr. 36(9-10): 443-452, 1978. Translation.

Carson, J. and C. Erikson, "Results from Survey of Environmental Tobacco Smoke in Offices in Ottawa, Ontario," Environ. Technol. Letters 9: 501-508, 1988.

Hinds, W. and M. First, "Concentrations of Nicotine and Tobacco Smoke in Public Places," New Eng. J. of Med. 292(16): 844-845, 1975.

Jenkins, R., et al., "Development and Application of a Thermal Desorption-Based Method for the Determination of Nicotine in Indoor Environments," Indoor and Ambient Air Quality, eds. R. Perry and P. Kirk, London, Selper Ltd.: 557-566, 1988.

Muramatsu, M., et al., "Estimation of Personal Exposure to Ambient Nicotine in Daily Environment," Arch. Occup. Environ. Health 59: 545-550, 1987.

3. White, J. and H. Froeb, "Small-Airways Dysfunction in Nonsmokers Chronically Exposed to Tobacco Smoke," New Eng. J. of Med. 302(13): 720-723, 1980.

2500061625

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

4. Adlkofer, F., et al., "Small-Airways Dysfunction in Passive Smokers," New Eng. J. of Med. 303(7): 392, 1980.

Huber, G., "Small-Airways Dysfunction in Passive Smokers," New Eng. J. of Med. 303(7): 392, 1980.

Freedman, A., "Small-Airways Dysfunction in Passive Smokers," New Eng. J. of Med. 303(7): 393, 1980.

Aviado, D., "Small-Airways Dysfunction in Passive Smokers," New Eng. J. of Med. 303(7): 393, 1980.

Fountain, L.H., "White-Froeb Study Discredited by Scientists," U.S. Cong. Record, Ninety-Seventh Congress, Second Session, Washington, D.C., U.S. Government Printing Office, E5252-5254, December 16, 1982.

Lebowitz, M., "Influence of Passive Smoking on Pulmonary Function: A Survey," Preventive Medicine 13(6): 645-655, 1984.

5. Kentner, M., et al., "The Influence of Passive Smoking on Pulmonary Function - A Study of 1,351 Office Workers," Preventive Medicine 13(6): 656-669. 1984.

Kentner, M. and D. Weltle, "Passive Tobacco Smoke Inhalation and Lung Function in Adults," Indoor and Ambient Air Quality, eds. R. Perry and P. Kirk, London, Selper Ltd.: 232-241, 1988.

6. Kabat, G. and E. Wynder, "Lung Cancer in Nonsmokers," Cancer 53(5): 1214-1221, 1984.

Garfinkel, L., et al., "Involuntary Smoking and Lung Cancer: A Case-Control Study," JNCI 75(3): 463-469, 1985.

Shimizu, H., et al., "A Case-Control Study of Lung Cancer in Nonsmoking Women," Tohoku J. Exp. Med. 154: 389-97, 1988.

Koo, L., et al., "Measurements of Passive Smoking and Estimates of Lung Cancer Risk Among Non-Smoking Chinese Females," Int. J. Cancer 39: 162-169, 1987.

Wu, A., et al., "Smoking and Other Risk Factors for Lung Cancer in Women," JNCI 74(4): 747-751, 1985.

Lee, P., et al., "Relationship of Passive Smoking to Risk of Lung Cancer and Other Smoking-Associated Diseases," Brit. J. Cancer 54: 97-105, 1986.

2500061626

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Svensson, C. et al., "Smoking and Passive Smoking in Relation to Lung Cancer in Women" Acta Oncologica 28: 623-629, 1989.

Wu-Williams, A., et al., "Lung Cancer Among Women in North-East China," Brit. J. of Cancer 62: 982-987, 1990.

Janerich, D. et al., "Lung Cancer and Exposure to Tobacco Smoke in the Household," New Eng. J. Med. 323(10): 632-636, 1990.

7. Lehrer, S., et al., "Tobacco Smoke Sensitivity: A Result of Allergy?," Ann Allergy 56: 1-10, 1986.

2500061627

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

II. SICK BUILDING SYNDROME

Because it is visible and easily identified by its aroma, environmental tobacco smoke is often blamed for indoor air quality problems. Government and private studies of "sick buildings" in the United States, Canada and Europe report, however, that tobacco smoke may be involved in only two percent to five percent of the buildings investigated for complaints about air quality.[1] For example, from 1981 through 1987, one company studied indoor air quality in 223 different buildings, accounting for over 39 million square feet of property, and found that ETS was a significant concern in only 10, or 4%, of the buildings [Robertson, 1988]. In another SBS database, smoking was implicated as a major contributor to complaints in only 12 of 408 (<3%) of the buildings surveyed [Collett, 1989]. The National Institute for Occupational Safety and Health (NIOSH) investigated more than 200 "sick" buildings and found that tobacco smoke was the source of claimed discomfort in only 2% of the buildings investigated. Ventilation problems were associated with half the complaints; outdoor air was considered a bigger problem than ETS [Melius, 1984]. Other investigators concluded that bacterial and fungal contamination is a major source of indoor air problems [Collett, 1989; Robertson, 1988].

2500061628

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

- Inadequate ventilation exacerbates all indoor air quality problems. This suggests that even a total smoking ban is not likely to affect comfort problems in 95 to 98 percent of "sick buildings."[2]

- The majority of indoor air quality problems in "sick buildings" have been traced to inadequate fresh air and poor air filtration. Because the visibility of tobacco smoke may be an indicator of inadequate ventilation, the prohibition of smoking serves to mask the real reason for poor indoor air quality--lack of proper ventilation. In addition, concentrating on tobacco smoke ignores the fact that adequate ventilation should always be provided in any enclosed space, regardless of whether or not smoking is permitted.

2500061629

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

REFERENCES

1. Kirkbride, J., "Sick Building Syndrome: Causes and Effects," Health and Welfare Canada, Ottawa, Canada, 1985.

Melius, J., et al., "Indoor Air Quality -- the NIOSH Experience," Ann. Am. Conf. Gov. Ind. Hydg. 10: 3-7, 1984.

Robertson, G., "Source, Nature and Symptomology on Indoor Air Pollutants," Indoor and Ambient Air Quality, eds. R. Perry and P. Kirk, London, Selper Ltd.: 311-319, 1988.

Collett, C. et al., "A Database of Problem Buildings: Learning by Past Mistakes," Present and Future of Indoor Air Quality, eds. C. Bieva et al.. Amsterdam, Elsevier Science Publishers: 413-419, 1989.

Turner, S. and P. Binnie, "An Indoor Air Quality Survey of Twenty-Six Swiss Office Buildings," Indoor Air '90, Toronto, Canada: 27-32, 1990.

2. Sterling, T. and Kleven, S., "The Epidemiology of 'Sick Public Buildings'," Indoor Air Quality: Symposium, Buenos Aires, National Academy of Sciences of Buenos Aires: 79-107, 1989.

2500061630

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

III. VENTILATION

- In 1981, The American Society of Heating, Refrigeration and Air-Conditioning Engineers (ASHRAE) issued a ventilation standard for public places (ASHRAE 62-1981).[1] The Standard established two levels of ventilation, one for areas in which smoking was permitted, and another substantially lower rate for areas where smoking was prohibited. The Standard was recently revised and reissued (ASHRAE 62-1989) with one prescribed ventilation rate, regardless of whether smoking was permitted or not. The decision to reject separate ventilation rates for smoking and nonsmoking areas was influenced by two areas of research: (1) The amount of ventilation required to remove indoor contaminants produced by humans, namely carbon dioxide and body odor, is also sufficient to remove typical amounts of ETS; and (2) ventilation rates for nonsmoking areas under ASHRAE 62-1981 were found to be inadequate and permitted airborne substances to increase, even in the absence of ETS.[2]

- Operating costs for increasing ventilation to meet specifications set forth in ASHRAE 62-1989 have been estimated at 3-5% over current annual energy expenditures for office buildings. Compliance with ASHRAE Standard 62-1989 will apparently have little effect on annual energy budgets.[3]

2500061631

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

REFERENCES

1. American Society of Heating, Refrigeration and Air Conditioning Engineers, ASHRAE Standard 62-1989, "Ventilation for Acceptable Indoor Air Quality," Atlanta, ASHRAE Publications, 1989.

2. Burroughs, H., "ASHRAE: Addressing the Indoor Air Quality Challenge With Energy Conscious Design," eds. R. Perry and P. Kirk, Indoor and Ambient Air Quality, London, Selper Ltd.: 530-535, 1988.

3. Eto, J., "The HVAC Costs of Increased Fresh Air Ventilation Rates in Office Buildings Part 2," Indoor Air '90, Toronto, Indoor Air '90: 53-58, 1990.

2500061632

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

IV. ACCOMMODATION

- Since the claim that exposure to tobacco smoke causes disease in nonsmokers is not scientifically justified,[1] the real issue regarding the "right" to smoke-free air is whether or not smoking should be prohibited because some people consider it to be an annoyance or nuisance.

Annoyance:

- Tobacco smoke may be an annoyance or nuisance to some people, but such complaints typically arise in poorly ventilated areas. Such complaints are most frequently associated with inadequate ventilation and to indoor substances other than ETS [See Section II: "Sick-Buildings"].

- Regulating a behavior such as smoking merely because some see it as an annoyance has undesirable consequences. Numerous individual behaviors could fall into the category of "annoyances," and to demand restrictions on all those potentially "annoying" behaviors is "to call for government regulation of everything."[2]

- Such regulations also reject the real possibility that people can work things out among themselves and may place a minority

2500061633

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

of individuals in the position to dictate what is "right" for everyone.

- The alternative to intrusive regulation is good manners, common courtesy and cooperation between smokers and nonsmokers. This alternative preserves the delicate balance of individual rights and allows for accommodation of everyone's desires.

2500061634

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

REFERENCES

1. Wu, J., "Summary and Concluding Remarks," Environmental Tobacco Smoke: Proceedings of the International Symposium at McGill University 1989, eds. D. Ecobichon and J. Wu, Lexington, Massachusetts, Lexington Books: 367-375, 1990.

Layard, M., "Environmental Tobacco Smoke and Cancer: The Epidemiologic Evidence," Environmental Tobacco Smoke: Proceedings 1989: 99-115, 1990.

Wexler, L., "Environmental Tobacco Smoke and Cardiovascular Disease: A Critique of the Epidemiological Literature and Recommendations for Future Research," Environmental Tobacco Smoke: Proceedings 1989: 139-152, 1990.

Witorsch, P., "Effects of ETS Exposure on Pulmonary Function and Respiratory Health in Adults," Environmental Tobacco Smoke: Proceedings 1989: 169-185, 1990.

Adlkofer, F., "Biological Effects After Exposure to ETS," Indoor Air Quality: Symposium, Buenos Aires, National Academy of Sciences of Buenos Aires: 61-76, 1989.

Gostomzyk, G., "Passive Smoking - Report on an International Symposium (23-25 October 1986)," Public Health 49: 212-215, 1987.

Wynder, E. and G. Kabat, "Health Care and Society: Environmental Tobacco Smoke and Lung Cancer," Present and Future of Indoor Air Quality, eds. C. Bieva et al., Amsterdam, Elsevier Science Publishers: 135-145, 1989.

2. Williams, W., "Cigarettes and Property Rights," Clearing the Air: Perspectives on Environmental Tobacco Smoke, ed. R. Tollison, Lexington, Massachusetts, D.C. Heath and Company: 39-52, 1988.

2500061635

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

The Separation Issue:

- The 1986 Report of the Surgeon General on ETS suggests that separation of smokers and nonsmokers is not effective in minimizing the nonsmoker's exposure to ETS. That claim was made without scientific support. Indeed, subsequent research indicates that simple separation of smokers and nonsmokers effectively minimizes ETS exposures for nonsmokers.[1-3]

- One recent study reported that the use of designated smoking areas reduced exposure to ETS by 95%.[1] Another study of a smoking-restricted office building reported that ambient nicotine in nonsmoking areas was virtually undetectable, suggesting that ETS had a negligible impact on the nonsmoking areas of the building.[2]

- Canadian researchers, in a series of reports, presented results on levels of ETS constituents in offices where smoking was regulated and unregulated. They reported no significant differences in average ETS constituent levels between nonsmoking offices that received recirculated air from designated smoking areas and nonsmoking offices that did not receive recirculated air.[3] They concluded:

> The results indicate that the provision of a designated, but not separately ventilated smoking area can effectively eliminate or

2500061636

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

The Separation Issue:

- The 1986 Report of the Surgeon General on ETS suggests that separation of smokers and nonsmokers is not effective in minimizing the nonsmoker's exposure to ETS. That claim was made without scientific support. Indeed, subsequent research indicates that simple separation of smokers and nonsmokers effectively minimizes ETS exposures for nonsmokers.[1-3]

- One recent study reported that the use of designated smoking areas reduced exposure to ETS by 95%.[1] Another study of a smoking-restricted office building reported that ambient nicotine in nonsmoking areas was virtually undetectable, suggesting that ETS had a negligible impact on the nonsmoking areas of the building.[2]

- Canadian researchers, in a series of reports, presented results on levels of ETS constituents in offices where smoking was regulated and unregulated. They reported no significant differences in average ETS constituent levels between nonsmoking offices that received recirculated air from designated smoking areas and nonsmoking offices that did not receive recirculated air.[3] They concluded:

> The results indicate that the provision of a designated, but not separately ventilated smoking area can effectively eliminate or

2500061637

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

drastically reduce most components of environmental tobacco smoke from nonsmoking offices.

- A federally-sponsored study of ETS in aircraft cabins indicat that separation of smokers and nonsmokers is an effective mea for reducing exposure to ETS.[4] The authors reported that ma ETS constituent concentrations in nonsmoking sections we: below the limit of detection. Similar results have bee reported in other studies.[5]

2500061638

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

ETS AND
RESPIRATORY DISEASES AND CONDITIONS
IN NONSMOKING ADULTS AND CHILDREN

VOLUME I

2500061639

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

TABLE OF CONTENTS

INTRODUCTION AND TABLE OF CONTENTS.....TABLE OF CONTENTS

PARENTAL SMOKING AND CHILDHOOD RESPIRATORY HEALTH..TAB A
MAJOR STUDIES..... A1-A39
CAMERON ET AL., 1973..... A1
HARLAP ET AL., 1974..... A2
COLLEY, 1974..... A3
COLLEY ET AL., 1974..... A4
LEBOWITZ ET AL., 1976..... A5
LEEDER ET AL., 1976..... A6
BINDER ET AL., 1976..... A7
KERREBIJN ET AL., 1977..... A8
RANTAKALLIO, 1978..... A9
SIMS ET AL., 1978..... A10
FERGUSSON ET AL., 1980..... A11
FERGUSSON ET AL., 1981..... A12
BONHAM ET AL., 1981..... A13
LOVE ET AL., 1981..... A14
CAMACHO ET AL., 1982..... A15
DODGE, 1982..... A16
FERRIS ET AL., 1983..... A17
SCHENKER ET AL., 1983..... A18
EKWO ET AL., 1983..... A19
GARDNER ET AL., 1984..... A20
WARE ET AL., 1984..... A21
FERGUSSON ET AL., 1985..... A22
PEDREIRA ET AL., 1985..... A23
TOMINAGA ET AL., 1985..... A24
WATKINS ET AL., 1986..... A25
BURCHFIEL ET AL., 1986..... A26
KERIGAN ET AL., 1986..... A27
SALZMAN ET AL., 1987..... A28
FLEMING ET AL., 1987..... A29
COGSWELL ET AL., 1987..... A30
TAYLOR ET AL., 1987..... A31
OGSTON ET AL., 1987..... A32
SOMERVILLE ET AL., 1988..... A33
CHEN, 1989..... A34
CORBO ET AL., 1989..... A35
NEUSPIEL ET AL., 1989..... A36
DOCKERY ET AL., 1989..... A37
OWNBY ET AL., 1988..... A38
MAJOR REVIEW: RUBIN & DAMUS, 1988..... A39

PARENTAL SMOKING AND CHILDHOOD LUNG FUNCTION..... B
MAJOR STUDIES..... B1-B28
MANDI ET AL., 1974..... B1
TAGER ET AL., 1976..... B2
SCHILLING ET AL., 1977..... B3

2500061640

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

YARNELL ET AL., 1979..... B4
TAGER ET AL., 1979..... B5
WEISS ET AL., 1980..... B6
SPEIZER ET AL., 1980..... B7
HASSELBLAD ET AL., 1981..... B8
LEBOWITZ ET AL., 1982..... B9
DODGE, 1982..... B10
EKWO ET AL., 1983..... B11
TAGER ET AL., 1983..... B12
TASHKIN ET AL., 1984..... B13
VEDAL ET AL., 1984..... B14
LEBOWITZ ET AL., 1984..... B15
SPINACI ET AL., 1985..... B16
BERKEY ET AL., 1986..... B17
TECULESCU ET AL., 1986..... B18
CHEN ET AL., 1986..... B19
BURCHFIEL ET AL., 1986..... B20
LEBOWITZ ET AL., 1987..... B21
LEBOWITZ ET AL., 1987..... B22
O'CONNOR ET AL., 1987..... B23
TSIMOYIANIS ET AL., 1987..... B24
GOLD ET AL., 1989..... B25
DOCKERY ET AL., 1989..... B26
KAUFFMANN ET AL., 1989..... B27
MAJOR REVIEW: WITORSCH & WITORSCH, 1989..... B28

PARENTAL SMOKING AND COMPROMISED CHILDREN..... C
MAJOR STUDIES..... C1-C18
LEEDER ET AL., 1976..... C1
GORTMAKER ET AL., 1982..... C2
FERGUSSON ET AL., 1985..... C3
HORWOOD ET AL., 1985..... C4
MURRAY ET AL., 1986..... C5
ANDERSON ET AL., 1987..... C6
EVANS ET AL., 1987..... C7
TOYOSHIMA ET AL., 1987..... C8
KERSHAW, 1987..... C9
MURRAY ET AL., 1988..... C10
SOMERVILLE ET AL., 1988..... C11
STRACHAN, 1988..... C12
OLDIGS ET AL., 1990..... C13
SHERMAN ET AL., 1990..... C14
WEITZMAN ET AL., 1990..... C15
RUBIN, 1990..... C16
GILLJAM ET AL., 1990..... C17
YOUNG ET AL., 1991..... C18

PARENTAL SMOKING AND OTITIS MEDIA IN CHILDREN..... D
MAJOR STUDIES..... D1-D13
SAID ET AL., 1978..... D1
VINTHER ET AL., 1982..... D2
KRAEMER ET AL., 1983..... D3

2500061641

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

BLACK, 1985..... D4
MOORHEAD, 1985..... D5
PUKANDER ET AL., 1985..... D6
FLEMING ET AL., 1987..... D7
KALLAIL ET AL., 1987..... D8
TAINIO ET AL., 1988..... D9
STRACHAN ET AL., 1989..... D10
ZIELHUIS ET AL., 1989..... D11
PUKANDER ET AL., 1990..... D12
STRACHAN, 1990..... D13

ETS AND ADULT RESPIRATORY HEALTH..... E
MAJOR STUDIES..... E1-E4
LEE ET AL., 1986..... E1
KOO ET AL., 1988..... E2
HOLE ET AL., 1989..... E3
KOO ET AL., 1990..... E4

ETS AND ADULT LUNG FUNCTION..... F
MAJOR STUDIES..... F1-F11
BOUHUYS ET AL., 1978..... F1
SHEPHARD ET AL., 1979..... F2
WHITE ET AL., 1980..... F3
COMSTOCK ET AL., 1981..... F4
KAUFFMANN ET AL., 1983..... F5
JONES ET AL., 1983..... F6
KENTNER ET AL., 1984..... F7
LEBOWITZ ET AL., 1985..... F8
HOSEIN ET AL., 1986..... F9
MASI ET AL., 1988..... F10
KALANDIDI ET AL., 1990..... F11

ETS AND COMPROMISED ADULTS..... G
MAJOR STUDIES..... G1-G9
STAHLE ET AL., 1978..... G1
SHEPHARD ET AL., 1979..... G2
DAHMS ET AL., 1981..... G3
ING ET AL., 1983..... G4
ROMER ET AL., 1983..... G5
KNIGHT ET AL., 1985..... G6
WIEDEMANN ET AL., 1986..... G7
STANKUS ET AL., 1988..... G8
BAILEY ET AL., 1990..... G9

CONFOUNDERS..... H
MAJOR STUDIES..... H1-H30
COLLEY, 1974..... H1
COLLEY ET AL., 1974..... H2
HOLMA ET AL., 1977..... H3
MELIA ET AL., 1977..... H4
MELIA ET AL., 1979..... H5
SPEIZER ET AL., 1980..... H6

2500061642

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

LEBOWITZ ET AL., 1982..... H7
NATIONAL INSTITUTES OF HEALTH, 1983..... H8
EKWO ET AL., 1983..... H9
LEBOWITZ ET AL., 1984..... H10
BERWICK ET AL., 1984..... H11
GARDNER ET AL., 1984..... H12
HARRINGTON ET AL., 1985..... H13
WATKINS ET AL., 1986..... H14
KERIGAN ET AL., 1986..... H15
STRACHAN ET AL., 1986..... H16
ANDERSON ET AL., 1987..... H17
FLEMING ET AL., 1987..... H18
MARTIN ET AL., 1987..... H19
KOO ET AL., 1988..... H20
MELIA ET AL., 1988..... H21
GOREN ET AL., 1988..... H22
NORDVALL ET AL., 1988..... H23
MITCHELL ET AL., 1989..... H24
POPE, 1989..... H25
OSBORNE ET AL., 1989..... H26
PLATT ET AL., 1989..... H27
BRUNEKREEF ET AL., 1989..... H28
BERWICK ET AL., 1989..... H29
HURWITZ ET AL., 1991..... H30

2500061643

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

Environmental Tobacco Smoke

and

Heart Disease

2500061644

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

ETS and Heart Disease

TABLE OF CONTENTS

References (alphabetical)

Provides an alphabetical list of the reports and reviews included in the notebook. Identifies the tab number in the appendices where each is located.

PAGE

Introduction 1

Provides a summary of the overall scope of relevant literature and a description of the organization of the notebook.

Epidemiological Reports and Reviews 3

Reports with original data 3

Identifies and summarizes the risk claims in the 11 epidemiological studies (13 reports) with data on ETS exposure in relation to heart disease incidence or mortality. For more detailed discussions and criticisms of these reports, see Appendix A.

Reviews claiming ETS-associated risk 7

Identifies and discusses the four primary articles which have reviewed the epidemiological literature and concluded that ETS exposure is causally related to heart disease in nonsmokers. The focus is on the meta-analyses by Wells (1988) and Glantz and Parmley (1991). Copies of these articles are in Appendix B.

Reviews emphasizing inconclusiveness of the data 11

Identifies and sets forth the conclusions from the major literature reviews that have judged that the data are inadequate to support a conclusion that ETS is related to heart disease in nonsmokers. The discussion includes the 1986 reports of the U.S. Surgeon General and of the National Academy of Sciences, three reports presented at international conferences in 1989 and 1990 dealing with

2500061645

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

this issue, and the conclusions of a review in a 1991 book devoted to ETS. Copies of these six publications are provided in Appendix C.

Studies Involving Exercise Performance, Heart Disease Patients and Biochemical Measurements 14

Identifies and comments on the significance of a variety of studies that discuss ETS in relation to heart disease, but which do not directly deal with rates or relative risks of heart disease. This includes three studies of exercise performance (1 in healthy subjects; 2 in heart patients); four reports of adverse effects of ETS on blood clotting and two reports claiming adverse effects on cholesterol levels in children of smoking parents.

Endnotes 20

Appendices

References

Identifies the articles consecutively by tab number as they appear in the appendices.

Appendix A

Copies of 13 reports, representing 11 epidemiological studies, presenting original data on ETS and heart disease risk. Includes summaries and criticisms for each report.

Appendix B

Copies of four reviews or meta-analyses claiming that ETS increases heart disease risk in nonsmokers.

Appendix C

Copies of six reviews concluding that the literature has not demonstrated an increased nonsmoker heart disease risk related to ETS exposure.

Appendix D

Copies of 12 articles reporting adverse effects of ETS on exercise performance or biochemical values. Short summaries are provided with each article.

2500061646

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

WORKPLACE SMOKING ISSUES

2500061647

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000

TABLE OF CONTENTS

Workplace Smoking Issues

I. HEALTH CLAIMS 1

Exposure 1
Lung Function 1
Lung Cancer 2
Allergy 2

References 3
Selected Studies . . . . . .A

II. SICK BUILDING SYNDROME 6

References 10
Selected Studies . . . . . .B

III. VENTILATION 9

References 10
Selected Studies C

IV. ACCOMMODATION 11

Annoyance 11

References 13

Separation 14

References 16
Selected Studies . . . . . .D

V. APPENDICES 18

Smokers Rights in the Workplace:
An Employees Guide

Smoking in the Workplace:
Some Considerations

Smoking in the Workplace:
Accommodating Diversity

VI. INDEX

2500061648

Source: https://www.industrydocuments.ucsf.edu/docs/xldk0000